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FILE 'SCISEARCH' ENTERED AT 16:02:35 ON 22 MAR 2002

FILE 'TOXCENTER' ENTERED AT 16:02:35 ON 22 MAR 2002

FILE 'USPATFULL' ENTERED AT 16:02:35 ON 22 MAR 2002

FILE 'USPAT2' ENTERED AT 16:02:35 ON 22 MAR 2002


```
=> s ara-c
  26 FILES SEARCHED...
L1       32650 ARA-C

=> s triacetyluridine
L2         124 TRIACETYLURIDINE

=> s s ribosyl cytosine
  27 FILES SEARCHED...
L3           0 S RIBOSYL CYTOSINE
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=> s ribosyl cytosine
L4           1 RIBOSYL CYTOSINE

=> s cytidine
L5       47462 CYTIDINE

=> s dihydrouridine
L6        1546 DIHYDROURIDINE

=> s Huntington or leigh or Alpers or epilepsy
L7      451086 HUNTINGTON OR LEIGH OR ALPERS OR EPILEPSY

=> s l2 and l7
L8           8 L2 AND L7

=> d l8 1-8 bib abs kwic

L8   ANSWER 1 OF 8  BIOSIS  COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN   2002:22885  BIOSIS
DN   PREV200200022885
TI   PN401 in combination with coenzyme Q10 or creatine protect mice against
     3-nitropropionic acid toxicity.
AU   Liu, L. S. (1); Hu, Z. Y. (1); Garcia, R. A. G. (1); Noble, M. M. (1); von
     Borstel, R. W. (1); Saydoff, J. A. (1)
CS   (1) Neuroscience Research, Pro-Neuron, Inc., Gaithersburg, MD USA
SO   Society for Neuroscience Abstracts, (2001) Vol. 27, No. 2, pp. 2575.
     print.
     Meeting Info.: 31st Annual Meeting of the Society for Neuroscience San
     Diego, California, USA November 10-15, 2001
     ISSN: 0190-5295.
DT   Conference
LA   English
AB   PN401 is triacetyluridine, a prodrug that allows efficient
     systemic delivery of uridine following oral administration. PN401 has been
     shown to protect against cell loss, behavioral impairment and mortality in
     the 3-nitropropionic acid (3NP) model of Huntington's disease.
     This study evaluates the interaction of creatine or CoQ on the effects of
     PN401 in the 3NP model. Swiss male mice 7-9 months old were given PN401,
     creatine or CoQ in their chow at 5, 2 and .02%, respectively. 3NP was
     given daily for 12 days at 40-60 mg/kg i.p. Experiment 1 included a dose
     response of PN401 in the chow at 2, 4 and 8%. PN401 at all doses decreased
     mortality, weight loss, and impairment on rotarod due to 3NP. Higher doses
     of 4 and 8% PN401 were required to attenuate hypoactivity due to 3NP.
     Based on decreased mortality and hypoactivity, it appears higher doses
     (between 4 and 8%) of PN401 provide a larger neuroprotective effect.
     Experiment 2 tested PN401 and/or creatine and experiment 3 tested PN401
     and/or CoQ on 3NP-induced toxicity. PN401 or CoQ decreased mortality.
     PN401 or CoQ, but not creatine, attenuated loss of body weight due to 3NP.
     PN401 or CoQ attenuated hypoactivity due to 3NP. However, PN401+creatine
     had a positive interaction to prevent hypoactivity due to 3NP. PN401 or
     CoQ decreased impairment on the rotarod due to 3NP. There was no
     significant positive interaction between PN401 and CoQ. These data support
     a neuroprotective role for PN401 or CoQ in the 3NP model. Oral PN401
     delivers a sufficient concentration of uridine to obtain robust
     neuroprotective effects in the 3NP model of mitochondrial dysfunction.
AB   PN401 is triacetyluridine, a prodrug that allows efficient
     systemic delivery of uridine following oral administration. PN401 has been
     shown to protect against cell loss, behavioral impairment and mortality in
     the 3-nitropropionic acid (3NP) model of Huntington's disease.
     This study evaluates the interaction of creatine or CoQ on the effects of
     PN401 in the 3NP model. Swiss.  .  .
IT   Major Concepts
        Pharmacology; Toxicology
IT   Parts, Structures, & Systems of Organisms
        mitochondria
IT   Diseases
```

Huntington's disease: nervous system disease; mitochondrial dysfunction: nervous system disease.

IT Chemicals & Biochemicals
3-nitropropionic acid: toxicity; PN401: neuroprotectant - drug, oral administration; coenzyme Q10: neuroprotectant - drug; creatine: neuroprotectant - drug

IT Alternate Indexing
Huntington's Disease (MeSH)

L8 ANSWER 2 OF 8 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2002:3814 BIOSIS
DN PREV200200003814
TI Oral uridine prodrug PN401 protects mice against azide toxicity in vivo: Studies on the mechanism of uridine neuroprotection in vitro.
AU Saydoff, J. A. (1); Liu, L. S. (1); Hu, Z. Y. (1); Noble, M. M. (1); Tandon, P. (1); Garcia, R. A. G. (1); von Borstel, R. W. (1)
CS (1) Neuroscience Research, Pro-Neuron, Inc, Gaithersburg, MD USA
SO Society for Neuroscience Abstracts, (2001) Vol. 27, No. 2, pp. 2360. print.
Meeting Info.: 31st Annual Meeting of the Society for Neuroscience San Diego, California, USA November 10-15, 2001
ISSN: 0190-5295.
DT Conference
LA English
AB The pyrimidine uridine forms the backbone of UDP-sugars that are required for glycosylation reactions. Pyrimidine derivatives are also critical for phospholipid and glycogen synthesis. De novo biosynthesis of uridine nucleotides is coupled to the respiratory chain via the mitochondrial enzyme dihydroorotate dehydrogenase. Therefore, symptoms of respiratory chain dysfunction may involve pyrimidine insufficiency. Neurodegenerative diseases such as Alzheimer's disease and **Huntington**'s disease are associated with decreased activity of cytochrome oxidase (COX). Azide inhibits respiratory chain function via inhibition of COX and ATPase, producing chemical hypoxia. PN401 is **triacetyluridine**, a prodrug that efficiently delivers uridine after oral administration. These studies tested the effect of PN401 on toxicity induced by azide infusion (s.c.) for 2 weeks. PN401 was administered orally or in the chow. Uridine derivative (measured as total uridine) content of selected tissues, activity and rotarod performance were measured. Histological evaluation and T-maze testing are underway. PN401 significantly decreased azide-induced weight loss, mortality and apoptotic cells in the cerebral cortex. Some tissues had an increased total uridine pool with PN401 treatment. Azide dose-dependently led to cell death in an in vitro chemical hypoxia model using human neural stem cells that were differentiated. The addition of >50 muM uridine was neuroprotective. Oral PN401 delivers a sufficient concentration of uridine in vivo to obtain robust protective effects in the azide-induced model of mitochondrial dysfunction.
AB. . . enzyme dihydroorotate dehydrogenase. Therefore, symptoms of respiratory chain dysfunction may involve pyrimidine insufficiency. Neurodegenerative diseases such as Alzheimer's disease and **Huntington**'s disease are associated with decreased activity of cytochrome oxidase (COX). Azide inhibits respiratory chain function via inhibition of COX and ATPase, producing chemical hypoxia. PN401 is **triacetyluridine**, a prodrug that efficiently delivers uridine after oral administration. These studies tested the effect of PN401 on toxicity induced by. . .

L8 ANSWER 3 OF 8 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2001:98331 BIOSIS
DN PREV200100098331
TI Oral pyrimidine treatment protects mice against striatal damage and behavioral impairment induced by 3-nitropropionic acid.
AU Saydoff, J. A. (1); Liu, L. S.; von Borstel, R. W.
CS (1) Pro Neuron Inc, Gaithersburg, MD USA
SO Society for Neuroscience Abstracts, (2000) Vol. 26, No. 1-2, pp. Abstract No.-579.6. print.

Meeting Info.: 30th Annual Meeting of the Society of Neuroscience New Orleans, LA, USA November 04-09, 2000 Society for Neuroscience . ISSN: 0190-5295.
DT Conference
LA English
SL English
AB De novo biosynthesis of uridine nucleotides is directly coupled to the respiratory chain via the mitochondrial enzyme dihydroorotate dehydrogenase, which utilizes ubiquinone as a cofactor. Symptoms of respiratory chain dysfunction in vivo may therefore involve pyrimidine deficits. Oral administration of PN401 (**triacetyluridine**) delivers much higher levels of uridine to the circulation than oral administration of uridine itself. **Huntington**'s disease (HD) involves progressive weight loss and neuronal loss especially in the striatum, substantia nigra and thalamus. HD is associated with decreased activity of mitochondrial succinate dehydrogenase (Complex II). This enzyme can be inhibited in animals by i.p. 3-nitropropionic acid (3NP). Mice were treated daily with i.p. 3NP or saline and p.o. PN401 b.i.d. 4g/kg or vehicle treatment began one day before 3NP. The vehicle + 3NP group had neuronal damage detected by silver staining in the striatum, substantia nigra and/or thalamus in 80% of the mice with 38% mortality. The 3NP + PN401 group had reduced (13% of mice in only one area) neuronal damage observed and there was no mortality. In two subsequent studies, 3NP also induced weight loss and behavioral impairment in rotarod and activity measurements. PN401 significantly decreased 3NP-induced weight loss and behavioral impairment in rotarod and activity measurements. Thus, oral PN401 treatment has neuroprotective effects in a model of mitochondrial dysfunction.
AB. . . ubiquinone as a cofactor. Symptoms of respiratory chain dysfunction in vivo may therefore involve pyrimidine deficits. Oral administration of PN401 (**triacetyluridine**) delivers much higher levels of uridine to the circulation than oral administration of uridine itself. **Huntington**'s disease (HD) involves progressive weight loss and neuronal loss especially in the striatum, substantia nigra and thalamus. HD is associated. . .
IT Major Concepts
Behavior; Nervous System (Neural Coordination)
IT Diseases
Huntington's disease: nervous system disease; behavioral impairment: behavioral and mental disorders
IT Chemicals & Biochemicals
3-nitropropionic acid: neurotoxin; PN401 [**triacetyluridine**]: neuroprotectant - drug; mitochondrial succinate dehydrogenase; pyrimidine: neuroprotectant activity, oral; uridine nucleotide: de novo synthesis
IT Alternate Indexing
Huntington's Disease (MeSH)

L8 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2002 ACS
AN 2000:608584 CAPLUS
DN 133:187987
TI Methods using pyrimidine-based nucleosides for treatment of mitochondrial disorders
IN Naviaux, Robert K.
PA The Regents of the University of California, USA
SO PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000050043	A1	20000831	WO 2000-US4663	20000223

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI,

SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1171137 A1 20020116 EP 2000-910321 20000223
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

PRAI US 1999-121588P P 19990223
WO 2000-US4663 W 20000223

OS MARPAT 133:187987

AB Methods are provided for the treatment of mitochondrial disorders. The methods include the administration of a pyrimidine-based nucleoside, e.g. **triacetyluridine**. Also provided are methods of reducing or eliminating symptoms assocd. with mitochondrial disorders. Mitochondrial disorders particularly appropriate for treatment include those attributable to a deficiency of one or more pyrimidines.

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB Methods are provided for the treatment of mitochondrial disorders. The methods include the administration of a pyrimidine-based nucleoside, e.g. **triacetyluridine**. Also provided are methods of reducing or eliminating symptoms assocd. with mitochondrial disorders. Mitochondrial disorders particularly appropriate for treatment include those attributable to a deficiency of one or more pyrimidines.

ST pyrimidine nucleoside deriv mitochondrial disorder treatment; **triacetyluridine** mitochondrial disorder treatment

IT Disease, animal
(**Alpers** syndrome; pyrimidine-based nucleoside for treatment of mitochondrial disorder)

IT Nervous system
(**Huntington**'s chorea; pyrimidine-based nucleoside for treatment of mitochondrial disorder)

IT Brain, disease
(**Leigh**'s disease; pyrimidine-based nucleoside for treatment of mitochondrial disorder)

IT Muscle, disease
(MERRF (myoclonic **epilepsy** assocd. with ragged-red muscle fibers); pyrimidine-based nucleoside for treatment of mitochondrial disorder)

IT Infection
(refractory **epilepsy** or Asperger syndrome or autism with declines during infection; pyrimidine-based nucleoside for treatment of mitochondrial disorder)

L8 ANSWER 5 OF 8 TOXCENTER COPYRIGHT 2002 ACS
AN 2001:304961 TOXCENTER
CP Copyright 2002 BIOSIS
DN PREV200200022885
TI PN401 in combination with coenzyme Q10 or creatine protect mice against 3-nitropropionic acid toxicity
AU Liu, L. S. (1); Hu, Z. Y. (1); Garcia, R. A. G. (1); Noble, M. M. (1); von Borstel, R. W. (1); Saydoff, J. A. (1)
CS (1) Neuroscience Research, Pro-Neuron, Inc., Gaithersburg, MD USA
SO Society for Neuroscience Abstracts, (2001) Vol. 27, No. 2, pp. 2575. print
Meeting Info.: 31st Annual Meeting of the Society for Neuroscience San Diego, California, USA November 10-15, 2001
ISSN: 0190-5295.
DT Conference
FS BIOSIS
OS BIOSIS 2002:22885
LA English
ED Entered STN: 20020101
Last Updated on STN: 20020226
AN 2001:304961 TOXCENTER
CP Copyright 2002 BIOSIS
AB PN401 is **triacetyluridine**, a prodrug that allows efficient

systemic delivery of uridine following oral administration. PN401 has been shown to protect against cell loss, behavioral impairment and mortality in the 3-nitropropionic acid (3NP) model of **Huntington**'s disease. This study evaluates the interaction of creatine or CoQ on the effects of PN401 in the 3NP model. Swiss male mice 7-9 months old were given PN401, creatine or CoQ in their chow at 5, 2 and .02%, respectively. 3NP was given daily for 12 days at 40-60 mg/kg i.p. Experiment 1 included a dose response of PN401 in the chow at 2, 4 and 8%. PN401 at all doses decreased mortality, weight loss, and impairment on rotarod due to 3NP. Higher doses of 4 and 8% PN401 were required to attenuate hypoactivity due to 3NP. Based on decreased mortality and hypoactivity, it appears higher doses (between 4 and 8%) of PN401 provide a larger neuroprotective effect. Experiment 2 tested PN401 and/or creatine and experiment 3 tested PN401 and/or CoQ on 3NP-induced toxicity. PN401 or CoQ decreased mortality. PN401 or CoQ, but not creatine, attenuated loss of body weight due to 3NP. PN401 or CoQ attenuated hypoactivity due to 3NP. However, PN401+creatine had a positive interaction to prevent hypoactivity due to 3NP. PN401 or CoQ decreased impairment on the rotarod due to 3NP. There was no significant positive interaction between PN401 and CoQ. These data support a neuroprotective role for PN401 or CoQ in the 3NP model. Oral PN401 delivers a sufficient concentration of uridine to obtain robust neuroprotective effects in the 3NP model of mitochondrial dysfunction.

AB PN401 is **triacetyluridine**, a prodrug that allows efficient systemic delivery of uridine following oral administration. PN401 has been shown to protect against cell loss, behavioral impairment and mortality in the 3-nitropropionic acid (3NP) model of **Huntington**'s disease. This study evaluates the interaction of creatine or CoQ on the effects of PN401 in the 3NP model. Swiss. . .

ST Major Concepts
Pharmacology; Toxicology

ST Parts, Structures, & Systems of Organisms
mitochondria

ST Diseases
Huntington's disease: nervous system disease; mitochondrial dysfunction: nervous system disease

ST Chemicals & Biochemicals
3-nitropropionic acid: toxicity; PN401: neuroprotectant - drug, oral administration; coenzyme Q10: neuroprotectant - drug; creatine: neuroprotectant - drug

ST Alternate Indexing
Huntington's Disease (MeSH)

ST Miscellaneous Descriptors
body weight regulation; hypoactivity regulation; mortality rate; Meeting Abstract

L8 ANSWER 6 OF 8 TOXCENTER COPYRIGHT 2002 ACS
AN 2001:304136 TOXCENTER
CP Copyright 2002 BIOSIS
DN PREV200200003814
TI Oral uridine prodrug PN401 protects mice against azide toxicity in vivo: Studies on the mechanism of uridine neuroprotection in vitro
AU Saydoff, J. A. (1); Liu, L. S. (1); Hu, Z. Y. (1); Noble, M. M. (1); Tandon, P. (1); Garcia, R. A. G. (1); von Borstel, R. W. (1)
CS (1) Neuroscience Research, Pro-Neuron, Inc, Gaithersburg, MD USA
SO Society for Neuroscience Abstracts, (2001) Vol. 27, No. 2, pp. 2360. print Meeting Info.: 31st Annual Meeting of the Society for Neuroscience San Diego, California, USA November 10-15, 2001
ISSN: 0190-5295.
DT Conference
FS BIOSIS
OS BIOSIS 2002:3814
LA English
ED Entered STN: 20020101
Last Updated on STN: 20020226
AN 2001:304136 TOXCENTER
CP Copyright 2002 BIOSIS

AB The pyrimidine uridine forms the backbone of UDP-sugars that are required for glycosylation reactions. Pyrimidine derivatives are also critical for phospholipid and glycogen synthesis. De novo biosynthesis of uridine nucleotides is coupled to the respiratory chain via the mitochondrial enzyme dihydroorotate dehydrogenase. Therefore, symptoms of respiratory chain dysfunction may involve pyrimidine insufficiency. Neurodegenerative diseases such as Alzheimer's disease and **Huntington**'s disease are associated with decreased activity of cytochrome oxidase (COX). Azide inhibits respiratory chain function via inhibition of COX and ATPase, producing chemical hypoxia. PN401 is **triacetyluridine**, a prodrug that efficiently delivers uridine after oral administration. These studies tested the effect of PN401 on toxicity induced by azide infusion (s.c.) for 2 weeks. PN401 was administered orally or in the chow. Uridine derivative (measured as total uridine) content of selected tissues, activity and rotarod performance were measured. Histological evaluation and T-maze testing are underway. PN401 significantly decreased azide-induced weight loss, mortality and apoptotic cells in the cerebral cortex. Some tissues had an increased total uridine pool with PN401 treatment. Azide dose-dependently led to cell death in an in vitro chemical hypoxia model using human neural stem cells that were differentiated. The addition of >50 muM uridine was neuroprotective. Oral PN401 delivers a sufficient concentration of uridine in vivo to obtain robust protective effects in the azide-induced model of mitochondrial dysfunction.

AB. . . enzyme dihydroorotate dehydrogenase. Therefore, symptoms of respiratory chain dysfunction may involve pyrimidine insufficiency. Neurodegenerative diseases such as Alzheimer's disease and **Huntington**'s disease are associated with decreased activity of cytochrome oxidase (COX). Azide inhibits respiratory chain function via inhibition of COX and ATPase, producing chemical hypoxia. PN401 is **triacetyluridine**, a prodrug that efficiently delivers uridine after oral administration. These studies tested the effect of PN401 on toxicity induced by. . .

L8 ANSWER 7 OF 8 USPATFULL
AN 2001:139534 USPATFULL
TI Compositions and methods for treatment of mitochondrial diseases
IN von Borstel, Reid W., Potomac, MD, United States
PA Pro-Neuron, Inc. (U.S. corporation)
PI US 2001016576 A1 20010823
AI US 2001-838136 A1 20010420 (9)
RLI Continuation of Ser. No. US 1998-144096, filed on 31 Aug 1998, PENDING
DT Utility
FS APPLICATION
LREP Nixon & Vanderhye P.C., 8th Floor, 1100 N. Glebe Rd., Arlington, VA, 22201
CLMN Number of Claims: 46
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1390
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Compounds, compositions, and methods are provided for treatment of disorders related to mitochondrial dysfunction. The methods comprise administering to a mammal a composition containing pyrimidine nucleotide precursors in amounts sufficient to treat symptoms resulting from mitochondrial respiratory chain deficiencies.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUMM . . . disorders involving inherited defective mitochondria, acquired mitochondrial dysfunction contributes to diseases, particularly neurodegenerative disorders associated with aging like Parkinson's, Alzheimer's, **Huntington**'s Diseases. The incidence of somatic mutations in mitochondrial DNA rises exponentially with age; diminished respiratory chain activity is found universally. . .
SUMM [0017] It is an object of the invention to provide compositions and methods for treatment and prevention of **epilepsy**.
DETD . . . the invention are short-chain (2 to 6 carbon atoms) fatty acid

esters of uridine or cytidine. Particularly advantageous compounds are **triacetyluridine** or triacetylcytidine. Such compounds have better oral bioavailabilty than the parent nucleosides, and are rapidly deacetylated following absorption after oral. . .

DETD . . . diseases associated with mutations or deletions of mitochondrial DNA include: MELAS: (Mitochondrial Encephalomyopathy Lactic Acidemia, and Stroke-like episodes. MERRF: Myoclonic **Epilepsy** with "Ragged Red" (muscle) Fibers NARP: Neurogenic muscle weakness, Ataxia and Retinitis Pigmentosa LHON: Leber's Hereditary Optic Neuropathy **Leigh**'s Syndrome (Subacute Necrotizing Encephalomyopathy) PEO: Progressive External Opthalmoplegia Kearns-Sayres Syndrome (PEO, pigmentary retinopathy, ataxia, and heart-block)

DETD . . . conjunction with these syndromes include cardiomyopathy, muscle weakness and atrophy, developmental delays (involving motor, language, cognitive or executive function), ataxia, **epilepsy**, renal tubular acidosis, peripheral neuropathy, optic neuropathy, autonomic neuropathy, neurogenic bowel dysfunction, sensorineural deafness, neurogenic bladder dysfunction, dilating cardiomyopathy, migraine,. . .

DETD [0119] **Epilepsy** is often present in patients with mitochondrial cytopathies, involving a range of seizure severity and frequency, e.g. absence, tonic, atonic,. . .

DETD [0134] **Huntington**'s Disease also involves mitochondrial dysfunction in affected brain regions, with cooperative interactions of excitotoxic stimulation and mitochondrial dysfunction contributing to. . .

DETD [0158] Example 5 illustrates the protective effect of oral **triacetyluridine** in protecting against taxol-induced neuropathy.

DETD [0183] Example 1: Treatment of a multisystem mitochondrial disorder with **triacetyluridine**

DETD [0185] After beginning treatment with 0.05 mg/kg/day of oral **triacetyluridine**, and for a duration of at least 6 months, this patient has not had seizures or migraines; her paresthesias related. . . to void spontaneously on most days, requiring catheterization only once or twice per week. After 6 weeks of treatment with **triacetyluridine**, this patient was able to walk a full mile, which she has been unable to do for the past two. . . tachycardia with a heart rate greater than 140 bpm occurred upon simple rise to stand, and after 6 weeks of **triacetyluridine**, tachycardia occurred only on hills and stairs. Her sensorium has cleared and memory deficits have improved markedly.

DETD [0188] The transient shortening of this patient's menstrual cycle is interpreted as an improvement of ovarian function caused by **triacetyluridine** in the face of excessive hormonal stimulation by which the neuroendocrine system was attempting to compensate for ovarian dysfunction. Feedback. . .

DETD [0189] Example 2: Treatment of refractory **epilepsy**

DETD [0190] An 11 year old boy had refractory **epilepsy** since age 4.5, apparently due to a multiple mitochondrial DNA deletion syndrome. In December 1997, his condition deteriorated, including 2 admissions to an intensive care unit for crescendo **epilepsy**. Even with aggressive regimens of standard anticonvulsive therapy, this patient was having 8 to 10 grand-mal seizures per night, leaving. . .

DETD [0191] In the first three days after beginning treatment with oral **triacetyluridine** (initially at a dose of 0.05 g/kg/day, and incrementally increased to 0.1 and then 0.24 glkg/day over the course of. . . some recurrence of seizures especially during episodes of infection, though at a much lower frequency than prior to treatment with **triacetyluridine**. This patient has been able to return to school and resume active participation in sports. His appetite, cognitive function, and. . .

DETD [0193] A 2 year-old girl, with **Leigh**'s Syndrome (subacute necrotizing encephalopathy) associated with severe Complex I deficiency, displayed renal tubular acidosis requiring intravenous administration of 25 mEq per day of sodium bicarbonate. Within several hours after beginning intragastric treatment with **triacetyluridine** at 0.1

g/mg/day, her renal tubular acidosis resolved and supplementary bicarbonate was no longer required to normalize blood pH. **Triacetyluridine** also resulted in rapid normalization of elevated circulating amino acid concentrations, and maintained lactic acid at low levels after withdrawal. . .

DETD [0195] A 4.5 year-old girl with **epilepsy**, ataxia, language delay, and fat intolerance, and dicarboxylic aciduria was treated with **triacetyluridine** at a daily dose of 0.1 to 0.3 g/kg/day. Such treatment resulted in a 50% decline in seizure frequency, improvement. . .

DETD . . . An additional group of 10 mice received injections of vehicle alone. One of the groups of taxol-treated mice received oral **triacetyluridine**, 4000 mg/kg b.i.d. Nine days after the initiation of taxol treatments, nociceptive sensory deficits were tested by determining tail-flick latency. . .

Group:	Tail flick latency
Control (no taxol)	10.8 .+-. 0.5 seconds
Taxol	16.0 .+-. 3.1 seconds
Taxol + **triacetyluridine**	11.9 .+-. 0.7 seconds

DETD [0199] Taxol treatment impaired responses to painful stimuli as an index of toxic sensory neuropathy. Oral **triacetyluridine** treatment significantly attenuated taxol-induced alterations in tail-flick latency.

CLM What is claimed is:

. . . in claim 20 wherein said congenital mitochondrial disease is selected from the group consisting of MELAS, LHON, MERRF, NARP, PEO, **Leigh**'s Disease, and Kearns-Sayres Syndrome.

25. A method as in claim 22 wherein said neurodegenerative disorder is **Huntington**'s Disease.

. . . as in claim 1 wherein said pathophysiological consequence of mitochondrial respiratory chain dysfunction is selected from the group consisting of **epilepsy**, peripheral neuropathy, optic neuropathy, autonomic neuropathy, neurogenic bowel dysfunction, sensorineural deafness, neurogenic bladder dysfunction, migraine, and ataxia.

L8 ANSWER 8 OF 8 USPATFULL
AN 2001:100342 USPATFULL
TI COMPOSITIONS AND METHODS FOR TREATMENT OF MITOCHONDRIAL DISEASES
IN VON BORSTEL, REID W., POTOMAC, MD, United States
PI US 2001005719 A1 20010628
AI US 1998-144096 A1 19980831 (9)
DT Utility
FS APPLICATION
LREP NIXON & VANDERHYE, 1100 N. GLEBE ROAD, 8TH FLOOR, ARLINGTON, VA, 22201
CLMN Number of Claims: 46
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1402
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Compounds, compositions, and methods are provided for treatment of disorders related to mitochondrial dysfunction. The methods comprise administering to a mammal a composition containing pyrimidine nucleotide precursors in amounts sufficient to treat symptoms resulting from mitochondrial respiratory chain deficiencies.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUMM . . . disorders involving inherited defective mitochondria, acquired mitochondrial dysfunction contributes to diseases, particularly neurodegenerative disorders associated with aging like Parkinson's, Alzheimer's, **Huntington**'s Diseases. The incidence of somatic

mutations in mitochondrial DNA rises exponentially with age; diminished respiratory chain activity is found universally. . .

SUMM [0016] It is an object of the invention to provide compositions and methods for treatment and prevention of **epilepsy**.

SUMM . . . the invention are short-chain (2 to 6 carbon atoms) fatty acid esters of uridine or cytidine. Particularly advantageous compounds are **triacetyluridine** or triacetylcytidine. Such compounds have better oral bioavailabilty than the parent nucleosides, and are rapidly deacetylated following absorption after oral. . .

SUMM [0103] MERRF: Myoclonic **Epilepsy** with "Ragged Red" (muscle) Fibers

SUMM [0106] **Leigh**'s Syndrome (Subacute Necrotizing Encephalomyopathy)

SUMM . . . conjunction with these syndromes include cardiomyopathy, muscle weakness and atrophy, developmental delays (involving motor, language, cognitive or executive function), ataxia, **epilepsy**, renal tubular acidosis, peripheral neuropathy, optic neuropathy, autonomic neuropathy, neurogenic bowel dysfunction, sensorineural deafness, neurogenic bladder dysfunction, dilating cardiomyopathy, migraine,. . .

SUMM [0120] **Epilepsy** is often present in patients with mitochondrial cytopathies, involving a range of seizure severity and frequency, e.g. absence, tonic, atonic,. . .

SUMM [0132] **Huntington**'s Disease also involves mitochondrial dysfunction in affected brain regions, with cooperative interactions of excitotoxic stimulation and mitochondrial dysfunction contributing to. . .

SUMM [0151] Example 5 illustrates the protective effect of oral **triacetyluridine** in protecting against taxol-induced neuropathy.

DETD Treatment of a Multisystem Mitochondrial Disorder with **Triacetyluridine**

DETD [0173] After beginning treatment with 0.05 mg/kg/day of oral **triacetyluridine**, and for a duration of at least 6 months, this patient has not had seizures or migraines; her paresthesias related. . . to void spontaneously on most days, requiring catheterization only once or twice per week. After 6 weeks of treatment with **triacetyluridine**, this patient was able to walk a full mile, which she has been unable to do for the past two. . . tachycardia with a heart rate greater than 140 bpm occurred upon simple rise to stand, and after 6 weeks of **triacetyluridine**, tachycardia occurred only on hills and stairs. Her sensorium has cleared and memory deficits have improved markedly.

DETD [0176] The transient shortening of this patient's menstrual cycle is interpreted as an improvement of ovarian function caused by **triacetyluridine** in the face of excessive hormonal stimulation by which the neuroendocrine system was attempting to compensate for ovarian dysfunction. Feedback. . .

DETD Treatment of Refractory **Epilepsy**

DETD [0177] An 11 year old boy had refractory **epilepsy** since age 4.5, apparently due to a multiple mitochondrial DNA deletion syndrome. In December 1997, his condition deteriorated, including 2 admissions to an intensive care unit for crescendo **epilepsy**. Even with aggressive regimens of standard anticonvulsive therapy, this patient was having 8 to 10 grand-mal seizures per night, leaving. . .

DETD [0178] In the first three days after beginning treatment with oral **triacetyluridine** (initially at a dose of 0.05 g/kg/day, and incrementally increased to 0.1 and then 0.24 g/kg/day over the course of. . . some recurrence of seizures especially during episodes of infection, though at a much lower frequency than prior to treatment with **triacetyluridine**. This patient has been able to return to school and resume active participation in sports. His appetite, cognitive function, and. . .

DETD [0179] A 2 year-old girl, with **Leigh**'s Syndrome (subacute necrotizing encephalopathy) associated with severe Complex I deficiency, displayed renal tubular acidosis requiring intravenous administration of 25 mEq per day of sodium bicarbonate. Within several hours after beginning intragastric treatment with **triacetyluridine** at 0.1

g/mg/day, her renal tubular acidosis resolved and supplementary bicarbonate was no longer required to normalize blood pH. **Triacetyluridine** also resulted in rapid normalization of elevated circulating amino acid concentrations, and maintained lactic acid at low levels after withdrawal. . .

DETD [0180] A 4.5 year-old girl with **epilepsy**, ataxia, language delay, and fat intolerance, and dicarboxylic aciduria was treated with **triacetyluridine** at a daily dose of 0.1 to 0.3 g/kg/day. Such treatment resulted in a 50% decline in seizure frequency, improvement. . .

DETD . . . An additional group of 10 mice received injections of vehicle alone. One of the groups of taxol-treated mice received oral **triacetyluridine**, 4000 mg/kg b.i.d. Nine days after the initiation of taxol treatments, nociceptive sensory deficits were tested by determining tail-flick latency. . . .

DETD [0186] Taxol+**triacetyluridine** 11.9.+-.0.7 seconds

DETD [0187] Taxol treatment impaired responses to painful stimuli as an index of toxic sensory neuropathy. Oral **triacetyluridine** treatment significantly attenuated taxol-induced alterations in tail-flick latency.

CLM What is claimed is:

. . . in claim 20 wherein said congenital mitochondrial disease is selected from the group consisting of MELAS, LHON, MERRF, NARP, PEO, **Leigh**'s Disease, and Kearns-Sayres Syndrome.

25. A method as in claim 22 wherein said neurodegenerative disorder is **Huntington**'s Disease.

. . . as in claim 1 wherein said pathophysiological consequence of mitochondrial respiratory chain dysfunction is selected from the group consisting of **epilepsy**, peripheral neuropathy, optic neuropathy, autonomic neuropathy, neurogenic bowel dysfunction, sensorineural deafness, neurogenic bladder dysfunction, migraine, and ataxia.

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=> s l1 and l7
L9          98 L1 AND L7

=> s mitochondrial or mitochondria
L10     743736 MITOCHONDRIAL OR MITOCHONDRIA

=> s l9 and l10
L11         14 L9 AND L10

=> d l11 1-14 bib abs kwic

L11  ANSWER 1 OF 14  USPATFULL
AN     2001:215064  USPATFULL
TI     Neurotrophic tetrahydroisoquinolines and tetrahydrothienopyridines, and
       related compositions and methods
IN     Macielag, Mark, Branchburg, NJ, United States
       Sui, Zhihua, Flemingtn, NJ, United States
       Walsh, Shawn, Somerville, NJ, United States
       Zhao, Boyo, Lansdale, PA, United States
PA     Ortho-McNeil Pharmaceutical, Inc., Raritan, NJ, United States (U.S.
       corporation)
PI     US 6323215          B1   20011127
AI     US 2000-592530           20000612 (9)
PRAI   US 1999-143098P     19990709 (60)
DT     Utility
FS     GRANTED
EXNAM  Primary Examiner: Huang, Evelyn Mei
CLMN   Number of Claims: 15
ECL    Exemplary Claim: 1
DRWN   1 Drawing Figure(s); 1 Drawing Page(s)
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LN.CNT 1410
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention provides compounds having the following general structure: ##STR1##

This invention also provides pharmaceutical compositions comprising same and methods of using these compositions to treat and prevent disorders characterized by neuronal damage.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
DETD . . . syndrome), motor neuron diseases including amyotrophic lateral sclerosis, degenerative ataxias, cortical basal degeneration, ALS-Parkinson's-Dementia complex of Guam, subacute sclerosing panencephalitis, **Huntington**'s disease, Parkinson's disease, synucleinopathies, primary progressive aphasia, striatonigral degeneration, Machado-Joseph disease/spinocerebellar ataxia type 3 and olivopontocerebellar degenerations, Gilles De La. . .
DETD . . . in brain, spinal cord, nerve damage, meningoradiculitis, and/or myelopathy; subacute combined degeneration; transverse myelitis; Leber's hereditary neuropathy; subacute necrotic encephalopathy (**Leigh** 's disease); **mitochondrial** encephalopathy with demyelination; metachromatic leukodystrophy; Krabbe's disease; Fabry's disease; adrenoleukodystrophy; neuromyelitis optica (Devic's syndrome); demyelinating Schwannopathies; cranial and peripheral neuropathies. . .
DETD . . . with 3 mL/well of assay medium [Leibovitz's L-15 medium plus 0.6% glucose, 1% FCS, 1% N-2 supplement (Gibco), 10 M **ara-C**, 10 mM Hepes, and penicillin/streptomycin/glutamine] containing either vehicle (DMSO, 1/200,000), positive control (24 ng/mL NGF) or test compound (50-250 nM).. . .

L11 ANSWER 2 OF 14 USPATFULL
AN 2001:194135 USPATFULL
TI 26934, a novel cytidine deaminase-like molecule and uses thereof
IN Meyers, Rachel A., Newton, MA, United States
Rudolph-Owen, Laura A., Jamaica Plain, MA, United States
PA Millennium Pharmaceuticals, Inc. (U.S. corporation)
PI US 2001036649 A1 20011101
AI US 2001-802371 A1 20010309 (9)
PRAI US 2000-188294P 20000310 (60)
DT Utility
FS APPLICATION
LREP ALSTON & BIRD LLP, BANK OF AMERICA PLAZA, 101 SOUTH TRYON STREET, SUITE 4000, CHARLOTTE, NC, 28280-4000
CLMN Number of Claims: 28
ECL Exemplary Claim: 1
DRWN 14 Drawing Page(s)
LN.CNT 4004
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Novel cytidine deaminase-like polypeptides, proteins, and nucleic acid molecules are disclosed. In addition to isolated, full-length cytidine deaminase-like proteins, the invention further provides isolated cytidine deaminase-like fusion proteins, antigenic peptides, and anti-cytidine deaminase-like antibodies. The invention also provides cytidine deaminase-like nucleic acid molecules, recombinant expression vectors containing a nucleic acid molecule of the invention, host cells into which the expression vectors have been introduced, and nonhuman transgenic animals in which an cytidine deaminase-like gene has been introduced or disrupted. Diagnostic, screening, and therapeutic methods utilizing compositions of the invention are also provided.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUMM . . . its natural substrates, cytidine and deoxycytidine, cytidine deaminases also catalyzes the deamination of cytosine nucleoside analogs including the antineoplastic agents **ARA-C**, dFdC, and 5-AZA-CdR. The deamination of these compounds results in a loss of their pharmacological activity. Cytidine deaminases may therefore. . .

DETD . . . disease (paralysis agitans), progressive supranuclear palsy, corticobasal degenration, multiple system atrophy, including striatonigral degenration, Shy-Drager syndrome, and olivopontocerebellar atrophy, and **Huntington** disease; spinocerebellar degenerations, including spinocerebellar ataxias, including Friedreich ataxia, and ataxia-telanglectasia, degenerative diseases affecting motor neurons, including amyotrophic lateral sclerosis. . . muscular atrophy; inborn errors of metabolism, such as leukodystrophies, including Krabbe disease, metachromatic leukodystrophy, adrenoleukodystrophy, Pelizaeus-Merzbacher disease, and Canavan disease, **mitochondrial** encephalomyopathies, including **Leigh** disease and other **mitochondrial** encephalomyopathies; toxic and acquired metabolic diseases, including vitamin deficiencies such as thiamine (vitamin B.sub.1) deficiency and vitamin B.sub.12 deficiency, neurologic. . .

DETD . . . of the cell) and intracellular domains (i.e., within the cell). When referring to membrane-bound proteins found in intracellular organelles (e.g., **mitochondria**, endoplasmic reticulum, peroxisomes and microsomes), non-transmembrane domains include those domains of the protein that reside in the cytosol (i.e., the cytoplasm), the lumen of the organelle, or the matrix or the intermembrane space (the latter two relate specifically to **mitochondria** organelles). The C-terminal amino acid residue of a non-transmembrane domain is adjacent to an N-terminal amino acid residue of a. . .

L11 ANSWER 3 OF 14 USPATFULL
AN 2001:97971 USPATFULL
TI Aliphatic propargylamines as cellular rescue agents
IN Durden, David, Saskatchewan, Canada
Paterson, Alick, Saskatchewan, Canada
Davis, Bruce, Saskatchewan, Canada
Dyck, Lillian, Saskatchewan, Canada
Yu, Peter, Saskatchewan, Canada
Li, Xinmin, Saskatchewan, Canada
Boulton, Alan, Saskatchewan, Canada
PA University of Saskatchewan, Saskatoon, Canada (non-U.S. corporation)
PI US 6251950 B1 20010626
AI US 1998-110548 19980706 (9)
RLI Division of Ser. No. US 1997-891904, filed on 14 Jul 1997, now patented, Pat. No. US 5840979, issued on 24 Nov 1998
DT Utility
FS GRANTED
EXNAM Primary Examiner: Barts, Samuel
LREP Synnestvedt & Lechner LLP
CLMN Number of Claims: 8
ECL Exemplary Claim: 1
DRWN 4 Drawing Figure(s); 2 Drawing Page(s)
LN.CNT 874
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to the use of a group of propargylamines of the general formula (I) ##STR1##

wherein R.sup.1 is hydrogen or CH.sub.3 and R.sup.2 is (CH.sub.2).sub.n CH.sub.3 and n is an integer from 0 to 16, and salts thereof, as cellular rescue agents in the treatment and prevention of diseases in which cell death occurs by apoptosis. Some of the compounds of formula I are novel. The invention is also directed to the use of these compounds in the treatment of these diseases, as well as to processes for the preparation of the compounds.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUMM . . . spinal cord and other nerve crush injuries) and chronic types (e.g. Alzheimer's disease, Parkinson's disease, Picks's disease, amyotrophic lateral sclerosis, **Huntington**'s disease, glaucoma, as well as idiopathic neuropathies) are responsible for enormous human suffering, are a burden on health care systems. . .

SUMM . . . that deprenyl can prevent apoptosis by a mechanism which

involves selective alterations in gene expression to block the loss of **mitochondrial** function which in turn would commit these cells to apoptosis. Deprenyl has also been shown to prevent N-(2-chloroethyl)-N-ethyl-2-bromobenzylamine (DSP-4)-induced degeneration. . .

SUMM . . . head trauma, Bell's palsy, spinal cord and other nerve crush injuries, Alzheimer's disease, Parkinson's disease, Pick's disease, amyotrophic lateral sclerosis, **Huntington**'s disease, multiple sclerosis, cardiac myopathies, nephropathy, retinopathy, diabetic complications, glaucoma, as well as idiopathic neuropathies.

DRWD FIG. 1a is a graph showing the dose-response relationship of inhibition by R-N-(2-heptyl)propargylamine (R-2HPA) of **Ara C** induced apoptosis.

DRWD FIG. 1b is a graph showing the dose-response relationship of inhibition by (R)-N-(2-heptyl)-N-methyl-propargylamine (R-2HMP) of **Ara C** induced apoptosis.

DRWD FIG. 1c is a graph showing the effect of R-2HMP, S-2HMP, R-deprenyl and S-deprenyl (all 10.sup.-7 M) on **Ara C** induced apoptosis.

DETD . . . of cerebellar granule cells (CGC) can be induced into apoptosis by the addition of a high concentration of cytosine arabinoside (**Ara C**) (Dessi et al., 1995) and it has been shown that this is a p53 dependent apoptosis (Enokido et al, 1996).. . .

DETD . . . glass in 35 mm petri dishes for 3 days and then used for experiments. 20 .mu.l aliquots of drug solutions (**Ara C**, anti-apoptotic drugs, drug vehicles) were added to the medium of the cultures. 24 Hours later the cultures were fixed with. . . with bis-benzamide. Normal and apoptotic nuclei were counted to a total of 90-120 cells per culture. The optimum concentration of **Ara C** was found to be 100 .mu.M. Concentrations in excess of 150 .mu.M caused detachment of the cultures.

DETD . . . methyl propargylamines (R-2HMP and S-2HMP) and deprenyls (R-deprenyl and S-deprenyl) (FIG. 1c). R-2HMP and R-deprenyl (10.sup.-7 M) completely blocked the **Ara C** induced apoptosis while S-2HMP and S-deprenyl (10.sup.-7 M) did not (FIG. 1c). From Table 1 one can confirm that S-2HPA. . .

DETD It is concluded that **Ara C** induced apoptosis in cultures of CGC can be blocked by the aliphatic secondary propargylamines of the invention. From the comparison. . . effect. Further examination has shown that the S-enantiomers are in fact antagonists of the anti-apoptotic action of the R-enantiomers (lines **Ara C**+R-2HMP+S-2HMP and **Ara C** +R-2HMP+S-2HPA of Table 1).

DETD TABLE 1

(S)-N-(2-heptyl)-N-methyl-propargylamine (S-2HMP)
and (S)-N-(2-heptyl)-propargylamine (S-2HPA)
antagonistic effect on antiapoptotic action of
(R)-N-(2-heptyl)-N-methyl-propargylamine (R-2HMP)

Treatment	Percent Apoptotic Nuclei
Control	4.2 .+-. 0.3
Ara C	14.6 .+-. 0.9
Control + R-2HMP	4.8 .+-. 0.7
Ara C + R-2HMP	6.3 .+-. 0.8*
Control + S-2HMP	5.0 .+-. 0.6
Ara C + S-2HMP	13.7 .+-. 1.1
Ara C + R-2HMP + S-2HMP	15.1 .+-. 0.9#
Control + S-2HPA	4.7 .+-. 0.7
Ara C + S-2HPA	14.2 .+-. 0.9
Ara C + R-2HMP + S-2HPA	13.8 .+-. 1.2#

Values represent the mean .+-. sem of 4 cultures.
Compounds were added at the following concentrations: **Ara C** , 100 .mu.M, R-2HMP, 100 nM; S-2HMP, 10 .mu.M; S-2HPA, 10 .mu.M.
*P < 0.05 compared to **Ara C** alone.
#P < 0.05 compared to **Ara C** + R-2HMP.

DETD The inhibition of the rat liver **mitochondrial** monoamine A and B activity by R- and S-enantiomers of the compounds of the invention and of the previously reported. . .

DETD TABLE 6

Inhibition of rat liver **mitochondrial** monoamine oxidase B activities by enantiomers of some aliphatic propargylamines and aliphatic N-methyl propargylamines in vitro
PE Comparison
(1.9 .times. 10.sup.-5 M) to. . .

L11 ANSWER 4 OF 14 USPATFULL
AN 2001:63493 USPATFULL
TI DNA encoding taurine and GABA transporters and uses thereof
IN Smith, Kelli E., Wayne, NJ, United States
Borden, Laurence A., Hackensack, NJ, United States
Weinshank, Richard L., Teaneck, NJ, United States
Hartig, Paul R., Pennington, NJ, United States
PA Synaptic Pharmaceutical Corporation, Paramus, NJ, United States (U.S. corporation)
PI US 6225115 B1 20010501
AI US 1999-343361 19990630 (9)
RLI Continuation-in-part of Ser. No. US 1994-233616, filed on 25 Apr 1994, now abandoned Continuation-in-part of Ser. No. WO 1993-US1959, filed on 4 Mar 1993 Continuation-in-part of Ser. No. US 1992-959936, filed on 13 Oct 1992, now abandoned Continuation-in-part of Ser. No. US 1992-847742, filed on 4 Mar 1992, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Ulm, John
LREP White, John P.Cooper & Dunham LLP
CLMN Number of Claims: 17
ECL Exemplary Claim: 1
DRWN 61 Drawing Figure(s); 49 Drawing Page(s)
LN.CNT 4924
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention provides isolated nucleic acid molecules encoding two mammalian GABA transporters, a mammalian taurine transporter and two human GABA transporters; methods of isolating these nucleic acid molecules and vectors comprising such nucleic acid molecules as well as mammalian cells comprising such vectors. Nucleic acid probes for detecting nucleic acid molecules encoding mammalian or human GABA transporters, or mammalian or human taurine transporters; antisense oligonucleotides complementary to any sequences of a nucleic acid molecule which encodes a mammalian GABA or taurine transporter or human GABA or taurine transporter; and antibodies to the mammalian GABA or taurine transporters, or human GABA or taurine transporters are provided. Pharmaceutical compounds related to mammalian GABA or taurine transporters and to human GABA or taurine transporters are provided. Nonhuman transgenic animals which express DNA encoding normal or mutant mammalian GABA or taurine transporters, or normal or mutant human GABA or taurine transporters are provided. Further provided are methods for determining substrate binding, detecting expression, drug screening, and treatments for alleviating abnormalities associated with mammalian GABA or taurine transporters, or human GABA or taurine transporters.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUMM . . . diazepam, and related benzodiazepines has proven extremely useful in the treatment of generalized anxiety (116) and in certain forms of **epilepsy** (86).
SUMM . . . Osmoregulation is essential to normal brain function and may also play a critical role in various pathophysiological states such as **epilepsy**, migraine, and ischemia. The primary mechanism by which neurons and glial cells regulate osmolarity is via the selective accumulation and. . .
DETD . . . composition described above effective to reduce expression of the GABA transporter by the subject. Examples of such abnormal conditions are **epilepsy** and generalized anxiety. This invention also provides a method of treating abnormalities which are alleviated by reduction of expression of. . .
DETD . . . composition described above effective to reduce expression of

the taurine transporter by the subject. Examples of such abnormal conditions are **epilepsy**, migraine, and ischemia.

DETD . . . the transporter and thereby alleviate the abnormal condition. Some examples of abnormal conditions associated with excess GABA transporter activity are **epilepsy** and generalized anxiety. Excess taurine transporter activity associated disorders are **epilepsy**, migraine, and ischemia.

DETD . . . GABA and taurine transporter structure and function provides a model for the development of drugs useful for the treatment of **epilepsy**, generalized anxiety, migraine, ischemia and other neurological disorders.

DETD . . . H]GABA.sup.3 (98.9 Ci/mmole) was obtained from New England Nuclear (Boston, Mass.). GABA, taurine, hypotaurine, poly-D-lysine hydrobromide (average molecular weight, 67,700), **ara-C** and .beta.-alanine, betaine and L-DABA (L-(2,4) diaminobutyric acid) were from Sigma Chemical Company (St. Louis, Mo.); guvacine, nipecotic acid, OH-nipecotic. . .

DETD . . . a plating density of 15.times.10.sup.6 Cells per 100 mm dish was employed; the medium was supplemented with insulin. Cytosine arabinoside (**ara-C**) was added to a final concentration of 10 .mu.M on day 2 or 3 to inhibit the proliferation of non-neuronal. . .

DETD . . . the role they play in regulating GABAergic activity, and may result in the development of novel therapeutic agents for anxiety, **epilepsy**, and other neuropsychiatric disorders.

DETD 46. Krnjevic, K. (1991) In: GABA Mechanisms in **Epilepsy**, ed. G. Tunnicliff and B. U. Raess, pp 47-87, Wiley-Liss, NY.

DETD 47. Krogsgaard-Larsen, P., Falch, E., Larsson, O. M., and Schousboe, A. (1987) GABA uptake inhibitors: relevance to antiepliептic drug research. **Epilepsy** Res. 1: 77-93.

DETD 55. Lombardini, J. B. (1988) Effects of taurine and **mitochondrial** metabolic inhibitors on ATP-dependent Ca.sup.2+ uptake in synaptosomal and **mitochondrial** subcellular fractions of rat retina. J. Neurochemistry 51: 200-205.

DETD 92. Schousboe, A., Larsson, O. M., and Krogsgaard-Larsen, P. (1991) In: GABA Mechanisms In **Epilepsy**, ed. G. Tunnicliff and B. U. Raess, pp 165-187, Wiley-Liss, NY.

DETD 105. Twyman, R. E. and Macdonald, R. L. (1991) In: GABA Mechanisms In **Epilepsy**, editors G. Tunnicliff and B. U. Raess, pp 89-104, Wiley-Liss, NY.

DETD . . . M. (1990) Neuronal discharge hypersynchrony and the intracranial water balance in relation to glutamic acid and taurine redistribution: Migraine and **epilepsy**. Prog. Clin. Biol. Res. 351: 1-20.

L11 ANSWER 5 OF 14 USPATFULL

AN 2000:105417 USPATFULL

TI Neurite growth regulatory factors

IN Schwab, Martin E., Zurich, Switzerland
Caroni, Pierenrico W., Zurich, Switzerland
Paganetti, Paolo A., Zurich, Switzerland

PA Erziehungsdirektion of the Canton Zurich, Zurich, Switzerland (non-U.S. corporation)

PI US 6103232 20000815

AI US 1995-464509 19950605 (8)

RLI Continuation of Ser. No. US 1989-401212, filed on 30 Aug 1989, now patented, Pat. No. US 5684133 which is a continuation-in-part of Ser. No. US 1988-267941, filed on 4 Nov 1988, now abandoned

DT Utility

FS Granted

EXNAM Primary Examiner: Hutzell, Paula K.; Assistant Examiner: Davis, Minh-Tam

LREP Pennie & Edmonds LLP

CLMN Number of Claims: 22

ECL Exemplary Claim: 1

DRWN 80 Drawing Figure(s); 32 Drawing Page(s)

LN.CNT 4223

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to methods of inducing neurite outgrowth in the central nervous system by antagonizing neural growth inhibitory factors. More particularly, the present invention is directed to use of antibodies to the central nervous system (CNS) myelin associated proteins; such antibodies can be used in the diagnosis and therapies of nerve damage resulting from trauma, infarction, and degenerative disorders of the CNS. In a specific embodiment of the invention, the monoclonal antibody IN-1 may be used to promote neurite outgrowth of nerve fibers over long distances in spinal cord lesions.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

DETD . . . to toxic agents, nutritional deficiency, paraneoplastic syndromes, and degenerative nerve diseases (including but not limited to Alzheimer's disease, Parkinson's disease, **Huntington**'s Chorea, amyotrophic lateral sclerosis, and progressive supra-nuclear palsy). In a specific embodiment, such molecules may be used to detect an. . .

DETD . . . treated with such inhibitory protein antagonists. Examples of such disorders include but are not limited to Alzheimer's Disease, Parkinsons' Disease, **Huntington**'s Chorea, amyotrophic lateral sclerosis, or progressive supranuclear palsy. Such antagonists may be used to promote the regeneration of CNS pathways,. . .

DETD . . . infarction, or degenerative disorders of the central nervous system which include but are not limited to Alzheimer's disease, Parkinson's disease, **Huntington**'s Chorea, amyotrophic lateral sclerosis, or progressive supranuclear palsy. For example, in one embodiment, CNS myelin associated inhibitory protein receptors, or. . .

DETD . . . 6:3031-3038). In order to suppress the growth of Schwann cells added together with the peripheral neurons, pulses of cytosine arabinoside (**Ara C**, 10.sup.-5 M) were given twice for 24 hours on the 2nd and 5th day of co-culture in some experiments. The. . .

DETD . . . were added to glial cells after 2-16 days in culture. Ganglionic Schwann cells and fibroblasts were eliminated by pulses of **Ara C** in some of the experiments. NGF (50 or 100 ng/ml) was added to the culture medium, leading to a rapid. . .

DETD . . . 7.4 (Quigley, 1976, J. Cell Biol. 71: 472-486). 20-40% sucrose interphase (C6 plasma membranes fraction) and 40-60% sucrose interphase (C6 **mitochondrial** fraction) were collected, washed in Hank's medium and resuspended in MEM.

L11 ANSWER 6 OF 14 USPATFULL

AN 2000:21663 USPATFULL

TI Chemokine .beta.-6 antagonists

IN Kreider, Brent L., Germantown, MD, United States
Ruben, Steven M., Olney, MD, United States
Olsen, Henrik S., Gaithersburg, MD, United States

PA Human Genome Sciences, Inc., Rockville, MD, United States (U.S. corporation)

PI US 6028169 20000222

AI US 1997-995156 19971219 (8)

PRAI US 1997-42269P 19970331 (60)

DT Utility

FS Granted

EXNAM Primary Examiner: Kemmerer, Elizabeth

LREP Sterne, Kessler, Goldstein & Fox P.L.L.C.

CLMN Number of Claims: 129

ECL Exemplary Claim: 1

DRWN 34 Drawing Figure(s); 29 Drawing Page(s)

LN.CNT 5814

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Human chemokine .beta.-6 agonist and antagonist polypeptides and DNA encoding such polypeptides and procedure for producing such polypeptides by recombinant technique are disclosed. The chemokine .beta.-6 antagonists of the present invention may be employed to treat rheumatoid arthritis, lung inflammation, allergy, asmtha, infectious diseases and to prevent inflammation and atherosclerosis. The chemokine .beta.-6

agonists may be employed to myeloprotect patients undergoing chemotherapy.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

DRWD FIG. 6 illustrates that Ck.beta.-6 protects HPP-CFC but not LPP-CFC from the cytotoxic effect of cytosine arabinoside (**Ara-C**) in vitro.

DETD . . . such as lesions of the corticospinal system; disorders of the basal ganglia or cerebellar disorders; hyperkinetic movement disorders such as **Huntington**'s Chorea and senile chorea; drug-induced movement disorders, such as those induced by drugs which block CNS dopamine receptors; hypokinetic movement. . . ataxia, cerebellar cortical degenerations, multiple systems degenerations (Mencel, Dejerine-Thomas, Shi-Drager, and Machado-Joseph); systemic disorders (Refsum's disease, abetalipoprotemia, ataxia, telangiectasia, and **mitochondrial** multi.system disorder); demyelinating core disorders, such as multiple sclerosis, acute transverse myelitis; and disorders of the motor unit' such as. . .

DETD . . . the irrelevant protein HG200-3-B (column 3). AFter 48 hours of incubation, one set of the above cultures received 50 mg/ml **Ara-C** and the incubation was then continued for an additional 24 hours. Cells were then harvested, washed three times with HBSS. . . was calculated as follows: Percent protection is expressed as number of colonies found in cultures incubated in the presence of **Ara-C** divided by the number of colonies found in cultures incubated without **Ara-C**.times.100. Data from one out of 3 experiments are shown in FIG. 6. All the samples were tested in duplicates.

L11 ANSWER 7 OF 14 USPATFULL

AN 2000:18418 USPATFULL

TI Treatment of CNS tumors with metalloprotease inhibitors

IN Schwab, Martin E., Zurich, Switzerland
Caroni, Pierenrico W., Zurich, Switzerland
Paganetti, Paolo A., Birmensdorferstr., Switzerland

PA Erziehungsdirektion of the Canton Zurich, Zurich, Switzerland (non-U.S. corporation)

PI US 6025333 20000215

AI US 1995-462312 19950605 (8)

RLI Division of Ser. No. US 1989-401212, filed on 30 Aug 1989 which is a continuation-in-part of Ser. No. US 1988-267941, filed on 4 Nov 1988, now abandoned

DT Utility

FS Granted

EXNAM Primary Examiner: Allen, Marianne P.; Assistant Examiner: Hayes, Robert C.

LREP Pennie & Edmonds LLP

CLMN Number of Claims: 10

ECL Exemplary Claim: 1

DRWN 89 Drawing Figure(s); 32 Drawing Page(s)

LN.CNT 4299

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to genes and their encoded proteins which regulate neurite growth and the diagnostic and therapeutic use of such proteins (termed herein neurite growth regulatory factors). The proteins of the present invention include central nervous system myelin associated proteins and metalloproteases associated with glioblastoma cells and other malignant tumors which can metastasize to the brain. The metalloproteases of the invention have value in the treatment of nerve damage and of degenerative disorders of the nervous system. The present invention is also directed to inhibitors of the metalloproteases. Such inhibitors in combination with the CNS myelin associated inhibitory proteins can be used in the treatment of malignant tumors.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

DETD . . . to toxic agents, nutritional deficiency, paraneoplastic syndromes, and degenerative nerve diseases (including but not limited to

Alzheimer's disease, Parkinson's disease, **Huntington**'s Chorea, amyotrophic lateral sclerosis, and progressive supra-nuclear palsy). In a specific embodiment, such molecules may be used to detect an. . .

DETD . . . treated with such inhibitory protein antagonists. Examples of such disorders include but are not limited to Alzheimer's Disease, Parkinsons' Disease, **Huntington**'s Chorea, amyotrophic lateral sclerosis, or progressive supranuclear palsy. Such antagonists may be used to promote the regeneration of CNS pathways,. . .

DETD . . . infarction, or degenerative disorders of the central nervous system which include but are not limited to Alzheimer's disease, Parkinson's disease, **Huntington**'s Chorea, amyotrophic lateral sclerosis, or progressive supranuclear palsy. For example, in one embodiment, CNS myelin associated inhibitory protein receptors, or. .

DETD . . . 6:3031-3038). In order to suppress the growth of Schwann cells added together with the peripheral neurons, pulses of cytosine arabinoside (**Ara C**, 10.sup.-5 M) were given twice for 24 hours on the 2nd and 5th day of co-culture in some experiments. The. . .

DETD . . . were added to glial cells after 2-10 days in culture. Ganglionic Schwann cells and fibroblasts were eliminated by pulses of **Ara C** in some of the experiments. NGF (50 or 100 ng/ml) was added to the culture medium, leading to a rapid. . .

DETD . . . 7.4 (Quigley, 1976, J. Cell Biol. 71: 472-486). 20-40% sucrose interphase (C6 plasma membranes fraction) and 40-60% sucrose interphase (C6 **mitochondrial** fraction) were collected, washed in Hank's medium and resuspended in MEM.

L11 ANSWER 8 OF 14 USPATFULL
AN 2000:1697 USPATFULL
TI Autoantibodies to neurotransmitter receptors
IN Rogers, Scott W., Salt Lake City, UT, United States
Gahring, Lorise C., Salt Lake City, UT, United States
Twyman, Roy E., Doylestown, PA, United States
PA University of Utah Research Foundation, Salt Lake City, UT, United States (U.S. corporation)
PI US 6010854 20000104
AI US 1997-887769 19970703 (8)
RLI Division of Ser. No. US 1994-345527, filed on 28 Nov 1994, now patented, Pat. No. US 5731410
DT Utility
FS Granted
EXNAM Primary Examiner: Duffy, Patricia A.
LREP Clayton, Howarth & Cannon, P.C.
CLMN Number of Claims: 14
ECL Exemplary Claim: 1
DRWN 8 Drawing Figure(s); 6 Drawing Page(s)
LN.CNT 1313
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A peptide containing 24 amino acid residues that binds to anti-neuronal-glutamate-receptor autoantibodies associated with Rasmussen's encephalitis and that blocks activation of the GluR3 subunit is described. Methods of making the peptide and treating Rasmussen's encephalitis are also disclosed. Autoantibodies to other glutamate receptor subunits are associated with paraneoplastic neurodegenerative disease, amyotrophic lateral sclerosis, and neurodegenerative disease of unknown diagnosis. Methods of screening patients and of monitoring patients being treated for these disorders and syndromes are further described.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUMM . . . linked to subsequent neuronal death. This excitotoxicity is thought to play a role in nervous system destruction after stroke, trauma, **epilepsy**, Alzheimer's disease, and **Huntington**'s disease.

DETD . . . other day using a growth medium consisting of DMEM, 10% horse serum, 30 mM glucose, and 0.5 mM glutamine. Arabinosylcytosine (

ARA-C) was added for 1 day during the first week in culture to suppress growth of non-neuronal cells. Electrophysiological experiments were. . .

DETD Some patients exhibit autoreactivity to cellular proteins such as nuclear or **mitochondrial** proteins that interfere with the specificity of the assay and can lead to false positives. To minimize this problem, sera. . .

L11 ANSWER 9 OF 14 USPATFULL

AN 1999:163462 USPATFULL

TI Polynucleotides encoding myeloid progenitor inhibitory factor-1 (MPIF-1) and polypeptides encoded thereby

IN Ruben, Steven M., Olney, MD, United States
Li, Haodong, Gaithersburg, MD, United States

PA Human Genome Sciences, Inc., Rockville, MD, United States (U.S. corporation)

PI US 6001606 19991214

AI US 1996-722719 19960930 (8)

RLI Continuation-in-part of Ser. No. US 1995-446881, filed on 5 May 1995, now abandoned which is a continuation-in-part of Ser. No. US 1995-465682, filed on 6 Jun 1995, now abandoned which is a continuation-in-part of Ser. No. US 1994-208339, filed on 8 Mar 1994, now patented, Pat. No. US 5504003 Ser. No. Ser. No. US 1995-468775, filed on 6 Jun 1995, now abandoned And Ser. No. WO 1996-US15592, filed on 27 Sep 1996 , said Ser. No. US 465682 which is a continuation-in-part of Ser. No. US 446881 , said Ser. No. US 468775 which is a continuation-in-part of Ser. No. US 446881

PRAI US 1995-4517P 19950929 (60)

DT Utility

FS Granted

EXNAM Primary Examiner: Mertz, Prema

LREP Sterne, Kessler, Goldstein & Fox, P.L.L.C.

CLMN Number of Claims: 74

ECL Exemplary Claim: 1

DRWN 53 Drawing Figure(s); 49 Drawing Page(s)

LN.CNT 6406

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB There are disclosed therapeutic compositions and methods using isolated nucleic acid molecules encoding a human myeloid progenitor inhibitory factor-1 (MPIF-1) polypeptide (previously termed MIP-3 and chemokine .beta.8(CK.beta.8 or ckb-8)); a human monocyte-colony inhibitory factor (M-CIF) polypeptide (previously termed MIP1-.gamma. and chemokine .beta.1(CK.beta.1 or ckb-1)), and a macrophage inhibitory protein-4 (MIP-4), as well as MPIF-1, M-CIF and/or MIP-4 polypeptides themselves, as are vectors, host cells and recombinant methods for producing the same.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

DRWD . . . effect of MPIF-1 on the 5-Fu-induced killing of LPP-CFC cells. FIG. 21B shows the myeloprotective effect of MPIF-1 on the **Ara -C** induced killing of LPP-CFC cells.

DETD . . . damage caused by, for example, radiation therapy or chemotherapy using cell-cycle active drugs, such as cytosine arabinoside, hydroxyurea, 5-Fu and **Ara-C**. Once the chemotherapeutic drug has cleared the patients system, it would be desirable to stimulate rapid amplification and differentiation of. . .

DETD . . . such as lesions of the corticospinal system; disorders of the basal ganglia or cerebellar disorders; hyperkinetic movement disorders such as **Huntington**'s Chorea and senile chorea; drug-induced movement disorders, such as those induced by drugs which block CNS dopamine receptors; hypokinetic movement. . . ataxia, cerebellar cortical degenerations, multiple systems degenerations (Mencel, Dejerine-Thomas, Shi-Drager, and Machado-Joseph); systemic disorders (Refsum's disease, abetalipoprotemia, ataxia, telangiectasia, and **mitochondrial** multisystem disorder); demyelinating core disorders, such as multiple sclerosis, acute transverse myelitis; and disorders of the motor unit' such as. . .

DETD Similar experiments were performed using the chemotherapeutic agent, **Ara-C** instead of 5-Fu. As shown in FIG. 21B, dramatic protection of LPP-CFC by both from wild type MPIF-1 and a. . . of this mutant). Thus, MPIF-1 is able to protect LPP-CFC from the cytotoxicity induced by both chemotherapeutic drugs, 5-Fu and **Ara-C**.

L11 ANSWER 10 OF 14 USPATFULL
AN 1998:147687 USPATFULL
TI Aliphatic propargylamines as cellular rescue agents
IN Durden, David, Saskatoon, Canada
Paterson, Alick, Saskatoon, Canada
Davis, Bruce, Saskatoon, Canada
Dyck, Lillian, Saskatoon, Canada
Yu, Peter, Saskatoon, Canada
Li, Xinmin, Saskatoon, Canada
Boulton, Alan, Saskatoon, Canada
PA University of Saskatchewan, Saskatoon, Canada (non-U.S. corporation)
PI US 5840979 19981124
AI US 1997-891904 19970714 (8)
DT Utility
FS Granted
EXNAM Primary Examiner: Burn, Brian M.
LREP Synnestvedt & Lechner
CLMN Number of Claims: 9
ECL Exemplary Claim: 1
DRWN 4 Drawing Figure(s); 2 Drawing Page(s)
LN.CNT 867
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to the use of a group of propargylamines of the general formula (I) ##STR1## wherein R.sup.1 is hydrogen or CH.sub.3 and R.sup.2 is (CH.sub.2).sub.n CH.sub.3 and n is an integer from 0 to 16, and salts thereof, as cellular rescue agents in the treatment and prevention of diseases in which cell death occurs by apoptosis. Some of the compounds of formula I are novel. The invention is also directed to the use of these compounds in the treatment of these diseases, as well as to processes for the preparation of the compounds.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUMM . . . spinal cord and other nerve crush injuries) and chronic types (e.g. Alzheimer's disease, Parkinson's disease, Picks's disease, amyotrophic lateral sclerosis, **Huntington**'s disease, glaucoma, as well as idiopathic neuropathies) are responsible for enormous human suffering, are a burden on health care systems. . .
SUMM . . . that deprenyl can prevent apoptosis by a mechanism which involves selective alterations in gene expression to block the loss of **mitochondrial** function which in turn would commit these cells to apoptosis. Deprenyl has also been shown to prevent N-(2-chloroethyl)-N-ethyl-2-bromobenzylamine (DSP-4)-induced degeneration. . .
SUMM . . . head trauma, Bell's palsy, spinal cord and other nerve crush injuries, Alzheimer's disease, Parkinson's disease, Pick's disease, amyotrophic lateral sclerosis, **Huntington**'s disease, multiple sclerosis, cardiac myopathies, nephropathy, retinopathy, diabetic complications, glaucoma, as well as idiopathic neuropathies.
DRWD FIG. 1a is a graph showing the dose-response relationship of inhibition by R-N-(2-heptyl)propargylamine (R-2HPA) of **Ara C** induced apoptosis.
DRWD FIG. 1b is a graph showing the dose-response relationship of inhibition by (R)-N-(2-heptyl)-N-methylpropargylamine (R-2HMP) of **Ara C** induced apoptosis.
DRWD FIG. 1c is a graph showing the effect of R-2HMP, S-2HMP, R-deprenyl and S-deprenyl (all 10.sup.-7 M) on **Ara C** induced apoptosis.
DETD . . . of cerebellar granule cells (CGC) can be induced into apoptosis by the addition of a high concentration of cytosine arabinoside (**Ara C**) (Dessi et al., 1995) and it has been shown that this is a p53 dependent apoptosis (Enokido et al, 1996).. . .

DETD . . . glass in 35 mm petri dishes for 3 days and then used for experiments. 20 .mu.l aliquots of drug solutions (**Ara C**, anti-apoptotic drugs, drug vehicles) were added to the medium of the cultures. 24 Hours later the cultures were fixed with. . . with bis-benzamide. Normal and apoptotic nuclei were counted to a total of 90-120 cells per culture. The optimum concentration of **Ara C** was found to be 100 .mu.M. Concentrations in excess of 150 .mu.M caused detachment of the cultures.

DETD . . . methyl propargylamines (R-2HMP and S-2HMP) and deprenyls (R-deprenyl and S-deprenyl) (FIG. 1c). R-2HMP and R-deprenyl (10.sup.-7 M) completely blocked the **Ara C** induced apoptosis while S-2HMP and S-deprenyl (10.sup.-7 M) did not (FIG. 1c). From Table 1 one can confirm that S-2HPA. . .

DETD It is concluded that **Ara C** induced apoptosis in cultures of CGC can be blocked by the aliphatic secondary propargylamines of the invention. From the comparison. . . effect. Further examination has shown that the S-enantiomers are in fact antagonists of the anti-apoptotic action of the R-enantiomers (lines **Ara C**+R-2HMP+S-2HMP and **Ara C** +R-2HMP+S-2HPA of Table 1).

DETD TABLE 1

(S)-N-(2-heptyl)-N-methyl-propargylamine (S-2HMP) and (S)-N-(2-heptyl)-propargylamine (S-2HPA) antagonistic effect on antiapoptotic action of (R)-N-(2-heptyl)-N-methyl-propargylamine (R-2HMP)

Treatment	Percent Apoptotic Nuclei
Control	4.2 .+-. 0.3
Ara C	14.6 .+-. 0.9
Control + R-2HMP	4.8 .+-. 0.7
Ara C + R-2HMP	6.3 .+-. 0.8*
Control + S-2HMP	5.0 .+-. 0.6
Ara C .+-. S-2HMP	13.7 .+-. 1.1
Ara C + R-2HMP .+-. S-2HMP	15.1 .+-. 0.9#
Control + S-2HPA	4.7 .+-. 0.7
Ara C + S-2HPA	14.2 .+-. 0.9
Ara C + R-2HMP + S-2HPA	13.8 .+-. 1.2#

Values represent the mean .+-. sem of 4 cultures.
Compounds were added at the following concentrations: **Ara C**, 100 .mu.M, R2HMP, 100 nM; S2HMP, 10 .mu.M; S2HPA, 10 .mu.M.
*P < 0.05 compared to **Ara C** alone.
#P < 0.05 compared to **Ara C** + R2HMP.

DETD The inhibition of the rat liver **mitochondrial** monoamine A and B activity by R- and S-enantiomers of the compounds of the invention and of the previously reported. . .

DETD TABLE 6

Inhibition of rat liver **mitochondrial** monoamine oxidase B activities by enantiomers of some aliphatic propargylamines and aliphatic N-methyl propargylamines in vitro

	PE	Comparison
	(1.9 .times. 10.sup.-5 M)	to. . .

L11 ANSWER 11 OF 14 USPATFULL

AN 1998:31115 USPATFULL

TI Peptide for blocking autoantibody-evoked activation of glutamate receptor type 3 (GLUR3)

IN Rogers, Scott W., Salt Lake City, UT, United States
Gahring, Lorise C., Salt Lake City, UT, United States
Twyman, Roy E., Sandy, UT, United States

PA University of Utah Research Foundation, Salt Lake City, UT, United States (U.S. corporation)
PI US 5731410 19980324
AI US 1994-345527 19941128 (8)
DT Utility
FS Granted
EXNAM Primary Examiner: Allen, Marianne P.; Assistant Examiner: Duffy, Patricia A.
LREP Thorpe, North & Western, L.L.P.
CLMN Number of Claims: 1
ECL Exemplary Claim: 1
DRWN 8 Drawing Figure(s); 6 Drawing Page(s)

AB A peptide containing 24 amino acid residues that binds to anti-neuronal-glutamate-receptor autoantibodies associated with Rasmussen's encephalitis and that blocks activation of the GluR3 subunit is described. Methods of making the peptide and treating Rasmussen's encephalitis are also disclosed. Autoantibodies to other glutamate receptor subunits are associated with paraneoplastic neurodegenerative disease, amyotrophic lateral sclerosis, and neurodegenerative disease of unknown diagnosis. Methods of screening patients and of monitoring patients being treated for these disorders and syndromes are further described.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUMM . . . linked to subsequent neuronal death. This excitotoxicity is thought to play a role in nervous system destruction after stroke, trauma, **epilepsy**, Alzheimer's disease, and **Huntington**'s disease.
DETD . . . other day using a growth medium consisting of DMEM, 10% horse serum, 30 mM glucose, and 0.5 mM glutamine. Arabinosylcytosine (**ARA-C**) was added for 1 day during the first week in culture to suppress growth of non-neuronal cells. Electrophysiological experiments were. . .
DETD Some patients exhibit autoreactivity to cellular proteins such as nuclear or **mitochondrial** proteins that interfere with the specificity of the assay and can lead to false positives. To minimize this problem, sera. . .

L11 ANSWER 12 OF 14 USPATFULL
AN 97:101884 USPATFULL
TI Neurite growth regulatory factors, antibodies thereto, and pharmaceutical compositions
IN Schwab, Martin E., Zurich, Switzerland
Caroni, Pierenrico W., Zurich, Switzerland
PA Erziehungsdirektion of the Canton Zurich, Zurich, Switzerland (non-U.S. corporation)
PI US 5684133 19971104
AI US 1989-401212 19890830 (7)
RLI Continuation-in-part of Ser. No. US 1988-267941, filed on 4 Nov 1988, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Hill, Jr., Robert J.; Assistant Examiner: Cermak, Shelly Guest
LREP Pennie & Edmonds
CLMN Number of Claims: 23
ECL Exemplary Claim: 1
DRWN 82 Drawing Figure(s); 32 Drawing Page(s)
LN.CNT 4086
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The CNS myelin associated proteins inhibit neurite outgrowth in nerve cells and neuroblastoma cells, and can also inhibit fibroblast spreading. Such inhibitory proteins include a 35,000 dalton and a 250,000 dalton molecular weight protein and analogs, derivatives, and fragments thereof. The CNS myelin associated inhibitory proteins may be used in the treatment of malignant tumors. The present invention is also directed to antibodies to the CNS myelin associated proteins; such antibodies can be used in the diagnosis and therapies of nerve damage resulting from trauma, infarction, and degenerative disorders of the central nervous system. In a specific embodiment of the invention, monoclonal antibody IN-1 may be used to promote regeneration of nerve fibers over long distances in spinal cord lesions.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
DETD . . . to toxic agents, nutritional deficiency, paraneoplastic syndromes, and degenerative nerve diseases (including but not limited to Alzheimer's disease, Parkinson's disease, **Huntington**'s Chorea, amyotrophic lateral sclerosis, and progressive supra-nuclear palsy). In

a specific embodiment, such molecules may be used to detect an. . .
DETD . . . treated with such inhibitory protein antagonists. Examples of such disorders include but are not limited to Alzheimer's Disease, Parkinsons' Disease, **Huntington**'s Chorea, amyotrophic lateral sclerosis, or progressive supranuclear palsy. Such antagonists may be used to promote the regeneration of CNS pathways,. . .
DETD . . . infarction, or degenerative disorders of the central nervous system which include but are not limited to Alzheimer's disease, Parkinson's disease, **Huntington**'s Chorea, amyotrophic lateral sclerosis, or progressive supranuclear palsy. For example, in one embodiment, CNS myelin associated inhibitory protein receptors, or. . .
DETD . . . 6:3031-3038). In order to suppress the growth of Schwann cells added together with the peripheral neurons, pulses of cytosine arabinoside (**Ara C**, 10.sup.-5 M) were given twice for 24 hours on the 2nd and 5th day of co-culture in some experiments. The. . .
DETD . . . were added to glial cells after 2-10 days in culture. Ganglionic Schwann cells and fibroblasts were eliminated by pulses of **Ara C** in some of the experiments. NGF (50 or 100 ng/ml) was added to the culture medium, leading to a rapid. . .
DETD . . . 7.4 (Quigley, 1976, J. Cell Biol. 71: 472-486). 20-40% sucrose interphase (C6 plasma membranes fraction) and 40-60% sucrose interphase (C6 **mitochondrial** fraction) were collected, washed in Hank's medium and resuspended in MEM.

L11 ANSWER 13 OF 14 USPATFULL
AN 97:73495 USPATFULL
TI DNA encoding rat taurine transporter and uses thereof
IN Smith, Kelli E., Wayne, NJ, United States
Weinshank, Richard L., New York, NY, United States
Borden, Laurence A., Hackensack, NJ, United States
Hartig, Paul R., Princeton, NJ, United States
PA Synaptic Pharmaceutical Corporation, Paramus, NJ, United States (U.S. corporation)
PI US 5658786 19970819
WO 9318143 19930916
AI US 1994-295814 19941219 (8)
WO 1993-US1959 19930304
19941219 PCT 371 date
19941219 PCT 102(e) date
RLI Continuation-in-part of Ser. No. US 1992-959936, filed on 13 Oct 1992, now abandoned which is a continuation-in-part of Ser. No. US 1992-847742, filed on 4 Mar 1992, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Walsh, Stephen; Assistant Examiner: Kaufman, Claire
LREP White, John P.
CLMN Number of Claims: 13
ECL Exemplary Claim: 1
DRWN 39 Drawing Figure(s); 37 Drawing Page(s)
LN.CNT 3815
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention provides isolated nucleic acid molecules encoding two mammalian GABA transporters, a mammalian taurine transporter and two human GABA transporters and methods of isolating these nucleic acid molecules. Further provided are vectors comprising the nucleic acid molecules as well as mammalian cells comprising such vectors, and antibodies directed to the GABA and taurine transporters. Nucleic acid probes useful for detecting nucleic acid molecules encoding GABA and taurine transporters are also provided. Antisense oligonucleotides complementary to any sequences of a nucleic acid molecule which encodes a GABA or taurine transporter are further provided. Pharmaceutical compounds related to GABA and taurine transporters are provided. Nonhuman transgenic animals which express DNA encoding a normal or a mutant GABA or taurine transporter are also provided. Further provided are methods for determining substrate binding, detecting expression,

drug screening, and treatments for alleviating abnormalities associated with GABA and taurine transporters.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . diazepam and related benzodiazepines has proven extremely useful in the treatment of generalized anxiety (77) and in certain forms of **epilepsy** (57).

SUMM . . . Osmoregulation is essential to normal brain function and may also play a critical role in various pathophysiological states such as **epilepsy**, migraine, and ischemia. The primary mechanism by which neurons and glial cells regulate osmolarity is via the selective accumulation and. . .

DETD . . . composition described above effective to reduce expression of the GABA transporter by the subject. Examples of such abnormal conditions are **epilepsy** and generalized anxiety. This invention also provides a method of treating abnormalities which are alleviated by reduction of expression of. . . composition described above effective to reduce expression of the taurine transporter by the subject. Examples of such abnormal conditions are **epilepsy**, migraine, and ischemia.

DETD . . . the transporter and thereby alleviate the abnormal condition. Some examples of abnormal conditions associated with excess GABA transporter activity are **epilepsy** and generalized anxiety. Excess taurine transporter activity associated disorders are **epilepsy**, migraine, and ischemia.

DETD . . . GABA and taurine transporter structure and function provides a model for the development of drugs useful for the treatment of **epilepsy**, generalized anxiety, migraine, ischemia and other neurological disorders.

DETD . . . a plating density of 15.times.10.sup.6 cells per 100 mm dish was employed; the medium was supplemented with insulin. Cytosine arabinoside (**ara-C**) was added to a final concentration of 10 .mu.M on day 2 or 3 to inhibit the proliferation of non-neuronal. . .

DETD 35. Krnjevic, K. (1991) in GABA Mechanisms in **Epilepsy**, ed. G. Tunnicliff and B. U. Raess, pp 47-87, Wiley-Liss, NY.

DETD 36. Krogsgaard-Larsen, P., Falch, E., Larsson, O. M., and Schousboe, A. (1987) **Epilepsy** Res. 1, 77-93.

DETD 41. Lombardini, J. B. (1988) Effects of taurine and **mitochondrial** metabolic inhibitors on ATP-dependent Ca.sup.2+ uptake in synaptosomal and **mitochondrial** subcellular fractions of rat retina, J. Neurochemistry 51, 200-205.

DETD 62. Schousboe, A., Larsson, O. M., and Krogsgaard-Larsen, P. (1991) in GABA Mechanisms in **Epilepsy**, ed. G. Tunnicliff and B. U. Raess, pp 165-187, Wiley-Liss, NY.

DETD 73. Twyman, R. E. and Macdonald, R. L. (1991) in GABA Mechanisms in **Epilepsy**, editors G. Tunnicliff and B. U. Raess, pp 89-104, Wiley-Liss, NY.

DETD . . . N. M. Neuronal discharge hypersynchrony and the intracranial water balance in relation to glutamic acid and taurine redistribution: Migraine and **epilepsy**. Prog. Clin. Biol. Res. 351:1-20 (1990).

L11 ANSWER 14 OF 14 USPATFULL

AN 93:82731 USPATFULL

TI Diagnostic methods using neurite growth regulatory factors

IN Schwab, Martin E., Zurich, Switzerland
Caroni, Pierenrico W., Zurich, Switzerland
Paganetti, Paolo A., Zurich, Switzerland

PA Erziehungsdirektion of the Canton Zurich, Zurich, Switzerland (non-U.S. corporation)

PI US 5250414 19931005

AI US 1991-719692 19910624 (7)

RLI Continuation-in-part of Ser. No. US 1989-401212, filed on 30 Aug 1989 which is a continuation-in-part of Ser. No. US 1988-267941, filed on 4 Nov 1988, now abandoned

DT Utility

FS Granted

EXNAM Primary Examiner: Hill, Jr., Robert J.; Assistant Examiner: Cermak, Shelly Guest
LREP Pennie & Edmonds
CLMN Number of Claims: 17
ECL Exemplary Claim: 1
DRWN 96 Drawing Figure(s); 41 Drawing Page(s)
LN.CNT 5260
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The proteins of the present invention include central nervous system myelin associated proteins and metalloproteases associated with glioblastoma cells and other malignant tumors which can metastasize to the brain. The CNS myelin associated proteins inhibit neurite outgrowth in nerve cells and neuroblastoma cells, and can also inhibit fibroblast spreading. Such inhibitory proteins include a 35,000 dalton and a 250,000 dalton molecular weight protein. The CNS myelin associated inhibitory proteins may be used in the treatment of malignant tumors. Antibodies to the CNS myelin associated proteins can be used in the diagnosis and therapies of nerve damage. Monoclonal antibody IN-1 may be used to promote regeneration of nerve fibers over long distances in spinal cord lesions. The metalloproteases of the invention have value in diagnosis of malignancies and the treatment of nerve damage and degenerative disorders of the nervous system. Inhibitors of the metalloproteases in combination with the CNS myelin associated inhibitory proteins can be used in the treatment of malignant tumors. Methods of determining malignant potential of a cell by measuring metalloprotease activity are provided.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
DETD . . . to toxic agents, nutritional deficiency, paraneoplastic syndromes, and degenerative nerve diseases (including but not limited to Alzheimer's disease, Parkinson's disease, **Huntington**'s Chorea, amyotrophic lateral sclerosis, progressive supra-nuclear palsy, and other dementias). In a specific embodiment, such molecules may be used to. . .

DETD . . . treated with such inhibitory protein antagonists. Examples of such disorders include but are not limited to Alzheimer's Disease, Parkinsons' Disease, **Huntington**'s Chorea, amyotrophic lateral sclerosis, progressive supranuclear palsy and other dementias. Such antagonists may be used to promote the regeneration of. . .

DETD . . . infarction, or degenerative disorders of the central nervous system which include but are not limited to Alzheimer's disease, Parkinson's disease, **Huntington**'s Chorea, amyotrophic lateral sclerosis, or progressive supranuclear palsy. For example, in one embodiment, CNS myelin associated inhibitory protein receptors, or. . .

DETD . . . 6:3031-3038). In order to suppress the growth of Schwann cells added together with the peripheral neurons, pulses of cytosine arabinoside (**Ara C**, 10.sup.-5 M) were given twice for 24 hours on the 2nd and 5th day of co-culture in some experiments. The. . .

DETD . . . were added to glial cells after 2-10 days in culture. Ganglionic Schwann cells and fibroblasts were eliminated by pulses of **Ara C** in some of the experiments. NGF (50 or 100 ng/ml) was added to the culture medium, leading to a rapid. . .

DETD . . . 7.4 (Quigley, 1976, J. Cell Biol. 71: 472-486). 20-40% sucrose interphase (C6 plasma membranes fraction) and 40-60% sucrose interphase (C6 **mitochondrial** fraction) were collected, washed in Hank's medium and resuspended in MEM.

DETD . . . centrifuged at 80,000.times.g for 1 h in a Beckman SW28 motor. Plasma membranes were harvested at the top and the **mitochondrial** fraction at the interphase of this 2 step gradient. Both fractions were diluted 10.times. with CMF-Hank's and pelleted (Beckman TI80,. . .

DETD . . . fractions. Maximal activity was associated with the plasma membrane (2.7 nMol/min). On the other hand, crude homogenate (0.08 nMol/min) and **mitochondrial** fraction (0.27 nMol/min) were clearly less active. No activity was found in C6 cell conditioned medium (0.03 nMol/min (FIG. 30a).. . .

```
=> s l4 or l5 or l6
L12       48804 L4 OR L5 OR L6

=> s l7 and l12
  29 FILES SEARCHED...
L13         344 L7 AND L12
```

AB A peptide containing 24 amino acid residues that binds to anti-neuronal-glutamate-receptor autoantibodies associated with Rasmussen's encephalitis and that blocks activation of the GluR3 subunit is described. Methods of making the peptide and treating Rasmussen's encephalitis are also disclosed. Autoantibodies to other glutamate receptor subunits are associated with paraneoplastic neurodegenerative disease, amyotrophic lateral sclerosis, and neurodegenerative disease of unknown diagnosis. Methods of screening patients and of monitoring patients being treated for these disorders and syndromes are further described.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUMM . . . linked to subsequent neuronal death. This excitotoxicity is thought to play a role in nervous system destruction after stroke, trauma, **epilepsy**, Alzheimer's disease, and **Huntington**'s disease.
DETD . . . other day using a growth medium consisting of DMEM, 10% horse serum, 30 mM glucose, and 0.5 mM glutamine. Arabinosylcytosine (**ARA-C**) was added for 1 day during the first week in culture to suppress growth of non-neuronal cells. Electrophysiological experiments were. . .
DETD Some patients exhibit autoreactivity to cellular proteins such as nuclear or **mitochondrial** proteins that interfere with the specificity of the assay and can lead to false positives. To minimize this problem, sera. . .

L11 ANSWER 12 OF 14 USPATFULL
AN 97:101884 USPATFULL
TI Neurite growth regulatory factors, antibodies thereto, and pharmaceutical compositions
IN Schwab, Martin E., Zurich, Switzerland
Caroni, Pierenrico W., Zurich, Switzerland
PA Erziehungsdirektion of the Canton Zurich, Zurich, Switzerland (non-U.S. corporation)
PI US 5684133 19971104
AI US 1989-401212 19890830 (7)
RLI Continuation-in-part of Ser. No. US 1988-267941, filed on 4 Nov 1988, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Hill, Jr., Robert J.; Assistant Examiner: Cermak, Shelly Guest
LREP Pennie & Edmonds
CLMN Number of Claims: 23
ECL Exemplary Claim: 1
DRWN 82 Drawing Figure(s); 32 Drawing Page(s)
LN.CNT 4086
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The CNS myelin associated proteins inhibit neurite outgrowth in nerve cells and neuroblastoma cells, and can also inhibit fibroblast spreading. Such inhibitory proteins include a 35,000 dalton and a 250,000 dalton molecular weight protein and analogs, derivatives, and fragments thereof. The CNS myelin associated inhibitory proteins may be used in the treatment of malignant tumors. The present invention is also directed to antibodies to the CNS myelin associated proteins; such antibodies can be used in the diagnosis and therapies of nerve damage resulting from trauma, infarction, and degenerative disorders of the central nervous system. In a specific embodiment of the invention, monoclonal antibody IN-1 may be used to promote regeneration of nerve fibers over long distances in spinal cord lesions.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
DETD . . . to toxic agents, nutritional deficiency, paraneoplastic syndromes, and degenerative nerve diseases (including but not limited to Alzheimer's disease, Parkinson's disease, **Huntington**'s Chorea, amyotrophic lateral sclerosis, and progressive supra-nuclear palsy). In

a specific embodiment, such molecules may be used to detect an. . .
DETD . . . treated with such inhibitory protein antagonists. Examples of such disorders include but are not limited to Alzheimer's Disease, Parkinsons' Disease, **Huntington**'s Chorea, amyotrophic lateral sclerosis, or progressive supranuclear palsy. Such antagonists may be used to promote the regeneration of CNS pathways,. . .
DETD . . . infarction, or degenerative disorders of the central nervous system which include but are not limited to Alzheimer's disease, Parkinson's disease, **Huntington**'s Chorea, amyotrophic lateral sclerosis, or progressive supranuclear palsy. For example, in one embodiment, CNS myelin associated inhibitory protein receptors, or. . .
DETD . . . 6:3031-3038). In order to suppress the growth of Schwann cells added together with the peripheral neurons, pulses of cytosine arabinoside (**Ara C**, 10.sup.-5 M) were given twice for 24 hours on the 2nd and 5th day of co-culture in some experiments. The. . .
DETD . . . were added to glial cells after 2-10 days in culture. Ganglionic Schwann cells and fibroblasts were eliminated by pulses of **Ara C** in some of the experiments. NGF (50 or 100 ng/ml) was added to the culture medium, leading to a rapid. . .
DETD . . . 7.4 (Quigley, 1976, J. Cell Biol. 71: 472-486). 20-40% sucrose interphase (C6 plasma membranes fraction) and 40-60% sucrose interphase (C6 **mitochondrial** fraction) were collected, washed in Hank's medium and resuspended in MEM.

L11 ANSWER 13 OF 14 USPATFULL
AN 97:73495 USPATFULL
TI DNA encoding rat taurine transporter and uses thereof
IN Smith, Kelli E., Wayne, NJ, United States
Weinshank, Richard L., New York, NY, United States
Borden, Laurence A., Hackensack, NJ, United States
Hartig, Paul R., Princeton, NJ, United States
PA Synaptic Pharmaceutical Corporation, Paramus, NJ, United States (U.S. corporation)
PI US 5658786 19970819
WO 9318143 19930916
AI US 1994-295814 19941219 (8)
WO 1993-US1959 19930304
19941219 PCT 371 date
19941219 PCT 102(e) date
RLI Continuation-in-part of Ser. No. US 1992-959936, filed on 13 Oct 1992, now abandoned which is a continuation-in-part of Ser. No. US 1992-847742, filed on 4 Mar 1992, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Walsh, Stephen; Assistant Examiner: Kaufman, Claire
LREP White, John P.
CLMN Number of Claims: 13
ECL Exemplary Claim: 1
DRWN 39 Drawing Figure(s); 37 Drawing Page(s)
LN.CNT 3815
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention provides isolated nucleic acid molecules encoding two mammalian GABA transporters, a mammalian taurine transporter and two human GABA transporters and methods of isolating these nucleic acid molecules. Further provided are vectors comprising the nucleic acid molecules as well as mammalian cells comprising such vectors, and antibodies directed to the GABA and taurine transporters. Nucleic acid probes useful for detecting nucleic acid molecules encoding GABA and taurine transporters are also provided. Antisense oligonucleotides complementary to any sequences of a nucleic acid molecule which encodes a GABA or taurine transporter are further provided. Pharmaceutical compounds related to GABA and taurine transporters are provided. Nonhuman transgenic animals which express DNA encoding a normal or a mutant GABA or taurine transporter are also provided. Further provided are methods for determining substrate binding, detecting expression,

drug screening, and treatments for alleviating abnormalities associated with GABA and taurine transporters.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . diazepam and related benzodiazepines has proven extremely useful in the treatment of generalized anxiety (77) and in certain forms of **epilepsy** (57).

SUMM . . . Osmoregulation is essential to normal brain function and may also play a critical role in various pathophysiological states such as **epilepsy**, migraine, and ischemia. The primary mechanism by which neurons and glial cells regulate osmolarity is via the selective accumulation and. . .

DETD . . . composition described above effective to reduce expression of the GABA transporter by the subject. Examples of such abnormal conditions are **epilepsy** and generalized anxiety. This invention also provides a method of treating abnormalities which are alleviated by reduction of expression of. . . composition described above effective to reduce expression of the taurine transporter by the subject. Examples of such abnormal conditions are **epilepsy**, migraine, and ischemia.

DETD . . . the transporter and thereby alleviate the abnormal condition. Some examples of abnormal conditions associated with excess GABA transporter activity are **epilepsy** and generalized anxiety. Excess taurine transporter activity associated disorders are **epilepsy**, migraine, and ischemia.

DETD . . . GABA and taurine transporter structure and function provides a model for the development of drugs useful for the treatment of **epilepsy**, generalized anxiety, migraine, ischemia and other neurological disorders.

DETD . . . a plating density of 15.times.10.sup.6 cells per 100 mm dish was employed; the medium was supplemented with insulin. Cytosine arabinoside (**ara-C**) was added to a final concentration of 10 .mu.M on day 2 or 3 to inhibit the proliferation of non-neuronal. . .

DETD 35. Krnjevic, K. (1991) in GABA Mechanisms in **Epilepsy**, ed. G. Tunnicliff and B. U. Raess, pp 47-87, Wiley-Liss, NY.

DETD 36. Krogsgaard-Larsen, P., Falch, E., Larsson, O. M., and Schousboe, A. (1987) **Epilepsy** Res. 1, 77-93.

DETD 41. Lombardini, J. B. (1988) Effects of taurine and **mitochondrial** metabolic inhibitors on ATP-dependent Ca.sup.2+ uptake in synaptosomal and **mitochondrial** subcellular fractions of rat retina, J. Neurochemistry 51, 200-205.

DETD 62. Schousboe, A., Larsson, O. M., and Krogsgaard-Larsen, P. (1991) in GABA Mechanisms in **Epilepsy**, ed. G. Tunnicliff and B. U. Raess, pp 165-187, Wiley-Liss, NY.

DETD 73. Twyman, R. E. and Macdonald, R. L. (1991) in GABA Mechanisms in **Epilepsy**, editors G. Tunnicliff and B. U. Raess, pp 89-104, Wiley-Liss, NY.

DETD . . . N. M. Neuronal discharge hypersynchrony and the intracranial water balance in relation to glutamic acid and taurine redistribution: Migraine and **epilepsy**. Prog. Clin. Biol. Res. 351:1-20 (1990).

L11 ANSWER 14 OF 14 USPATFULL

AN 93:82731 USPATFULL

TI Diagnostic methods using neurite growth regulatory factors

IN Schwab, Martin E., Zurich, Switzerland
Caroni, Pierenrico W., Zurich, Switzerland
Paganetti, Paolo A., Zurich, Switzerland

PA Erziehungsdirektion of the Canton Zurich, Zurich, Switzerland (non-U.S. corporation)

PI US 5250414 19931005

AI US 1991-719692 19910624 (7)

RLI Continuation-in-part of Ser. No. US 1989-401212, filed on 30 Aug 1989 which is a continuation-in-part of Ser. No. US 1988-267941, filed on 4 Nov 1988, now abandoned

DT Utility

FS Granted

EXNAM Primary Examiner: Hill, Jr., Robert J.; Assistant Examiner: Cermak, Shelly Guest
LREP Pennie & Edmonds
CLMN Number of Claims: 17
ECL Exemplary Claim: 1
DRWN 96 Drawing Figure(s); 41 Drawing Page(s)
LN.CNT 5260
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The proteins of the present invention include central nervous system myelin associated proteins and metalloproteases associated with glioblastoma cells and other malignant tumors which can metastasize to the brain. The CNS myelin associated proteins inhibit neurite outgrowth in nerve cells and neuroblastoma cells, and can also inhibit fibroblast spreading. Such inhibitory proteins include a 35,000 dalton and a 250,000 dalton molecular weight protein. The CNS myelin associated inhibitory proteins may be used in the treatment of malignant tumors. Antibodies to the CNS myelin associated proteins can be used in the diagnosis and therapies of nerve damage. Monoclonal antibody IN-1 may be used to promote regeneration of nerve fibers over long distances in spinal cord lesions. The metalloproteases of the invention have value in diagnosis of malignancies and the treatment of nerve damage and degenerative disorders of the nervous system. Inhibitors of the metalloproteases in combination with the CNS myelin associated inhibitory proteins can be used in the treatment of malignant tumors. Methods of determining malignant potential of a cell by measuring metalloprotease activity are provided.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
DETD . . . to toxic agents, nutritional deficiency, paraneoplastic syndromes, and degenerative nerve diseases (including but not limited to Alzheimer's disease, Parkinson's disease, **Huntington**'s Chorea, amyotrophic lateral sclerosis, progressive supra-nuclear palsy, and other dementias). In a specific embodiment, such molecules may be used to. . .

DETD . . . treated with such inhibitory protein antagonists. Examples of such disorders include but are not limited to Alzheimer's Disease, Parkinsons' Disease, **Huntington**'s Chorea, amyotrophic lateral sclerosis, progressive supranuclear palsy and other dementias. Such antagonists may be used to promote the regeneration of. . .

DETD . . . infarction, or degenerative disorders of the central nervous system which include but are not limited to Alzheimer's disease, Parkinson's disease, **Huntington**'s Chorea, amyotrophic lateral sclerosis, or progressive supranuclear palsy. For example, in one embodiment, CNS myelin associated inhibitory protein receptors, or. . .

DETD . . . 6:3031-3038). In order to suppress the growth of Schwann cells added together with the peripheral neurons, pulses of cytosine arabinoside (**Ara C**, 10.sup.-5 M) were given twice for 24 hours on the 2nd and 5th day of co-culture in some experiments. The. . .

DETD . . . were added to glial cells after 2-10 days in culture. Ganglionic Schwann cells and fibroblasts were eliminated by pulses of **Ara C** in some of the experiments. NGF (50 or 100 ng/ml) was added to the culture medium, leading to a rapid. . .

DETD . . . 7.4 (Quigley, 1976, J. Cell Biol. 71: 472-486). 20-40% sucrose interphase (C6 plasma membranes fraction) and 40-60% sucrose interphase (C6 **mitochondrial** fraction) were collected, washed in Hank's medium and resuspended in MEM.

DETD . . . centrifuged at 80,000.times.g for 1 h in a Beckman SW28 motor. Plasma membranes were harvested at the top and the **mitochondrial** fraction at the interphase of this 2 step gradient. Both fractions were diluted 10.times. with CMF-Hank's and pelleted (Beckman TI80,. . .

DETD . . . fractions. Maximal activity was associated with the plasma membrane (2.7 nMol/min). On the other hand, crude homogenate (0.08 nMol/min) and **mitochondrial** fraction (0.27 nMol/min) were clearly less active. No activity was found in C6 cell conditioned medium (0.03 nMol/min (FIG. 30a).. . .

```
=> s l4 or l5 or l6
L12       48804 L4 OR L5 OR L6

=> s l7 and l12
  29 FILES SEARCHED...
L13         344 L7 AND L12
```

AB A peptide containing 24 amino acid residues that binds to anti-neuronal-glutamate-receptor autoantibodies associated with Rasmussen's encephalitis and that blocks activation of the GluR3 subunit is described. Methods of making the peptide and treating Rasmussen's encephalitis are also disclosed. Autoantibodies to other glutamate receptor subunits are associated with paraneoplastic neurodegenerative disease, amyotrophic lateral sclerosis, and neurodegenerative disease of unknown diagnosis. Methods of screening patients and of monitoring patients being treated for these disorders and syndromes are further described.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUMM . . . linked to subsequent neuronal death. This excitotoxicity is thought to play a role in nervous system destruction after stroke, trauma, **epilepsy**, Alzheimer's disease, and **Huntington**'s disease.
DETD . . . other day using a growth medium consisting of DMEM, 10% horse serum, 30 mM glucose, and 0.5 mM glutamine. Arabinosylcytosine (**ARA-C**) was added for 1 day during the first week in culture to suppress growth of non-neuronal cells. Electrophysiological experiments were. . .
DETD Some patients exhibit autoreactivity to cellular proteins such as nuclear or **mitochondrial** proteins that interfere with the specificity of the assay and can lead to false positives. To minimize this problem, sera. . .

L11 ANSWER 12 OF 14 USPATFULL
AN 97:101884 USPATFULL
TI Neurite growth regulatory factors, antibodies thereto, and pharmaceutical compositions
IN Schwab, Martin E., Zurich, Switzerland
Caroni, Pierenrico W., Zurich, Switzerland
PA Erziehungsdirektion of the Canton Zurich, Zurich, Switzerland (non-U.S. corporation)
PI US 5684133 19971104
AI US 1989-401212 19890830 (7)
RLI Continuation-in-part of Ser. No. US 1988-267941, filed on 4 Nov 1988, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Hill, Jr., Robert J.; Assistant Examiner: Cermak, Shelly Guest
LREP Pennie & Edmonds
CLMN Number of Claims: 23
ECL Exemplary Claim: 1
DRWN 82 Drawing Figure(s); 32 Drawing Page(s)
LN.CNT 4086
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The CNS myelin associated proteins inhibit neurite outgrowth in nerve cells and neuroblastoma cells, and can also inhibit fibroblast spreading. Such inhibitory proteins include a 35,000 dalton and a 250,000 dalton molecular weight protein and analogs, derivatives, and fragments thereof. The CNS myelin associated inhibitory proteins may be used in the treatment of malignant tumors. The present invention is also directed to antibodies to the CNS myelin associated proteins; such antibodies can be used in the diagnosis and therapies of nerve damage resulting from trauma, infarction, and degenerative disorders of the central nervous system. In a specific embodiment of the invention, monoclonal antibody IN-1 may be used to promote regeneration of nerve fibers over long distances in spinal cord lesions.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
DETD . . . to toxic agents, nutritional deficiency, paraneoplastic syndromes, and degenerative nerve diseases (including but not limited to Alzheimer's disease, Parkinson's disease, **Huntington**'s Chorea, amyotrophic lateral sclerosis, and progressive supra-nuclear palsy). In

a specific embodiment, such molecules may be used to detect an. . .
DETD . . . treated with such inhibitory protein antagonists. Examples of such disorders include but are not limited to Alzheimer's Disease, Parkinsons' Disease, **Huntington**'s Chorea, amyotrophic lateral sclerosis, or progressive supranuclear palsy. Such antagonists may be used to promote the regeneration of CNS pathways,. . .
DETD . . . infarction, or degenerative disorders of the central nervous system which include but are not limited to Alzheimer's disease, Parkinson's disease, **Huntington**'s Chorea, amyotrophic lateral sclerosis, or progressive supranuclear palsy. For example, in one embodiment, CNS myelin associated inhibitory protein receptors, or. . .
DETD . . . 6:3031-3038). In order to suppress the growth of Schwann cells added together with the peripheral neurons, pulses of cytosine arabinoside (**Ara C**, 10.sup.-5 M) were given twice for 24 hours on the 2nd and 5th day of co-culture in some experiments. The. . .
DETD . . . were added to glial cells after 2-10 days in culture. Ganglionic Schwann cells and fibroblasts were eliminated by pulses of **Ara C** in some of the experiments. NGF (50 or 100 ng/ml) was added to the culture medium, leading to a rapid. . .
DETD . . . 7.4 (Quigley, 1976, J. Cell Biol. 71: 472-486). 20-40% sucrose interphase (C6 plasma membranes fraction) and 40-60% sucrose interphase (C6 **mitochondrial** fraction) were collected, washed in Hank's medium and resuspended in MEM.

L11 ANSWER 13 OF 14 USPATFULL
AN 97:73495 USPATFULL
TI DNA encoding rat taurine transporter and uses thereof
IN Smith, Kelli E., Wayne, NJ, United States
Weinshank, Richard L., New York, NY, United States
Borden, Laurence A., Hackensack, NJ, United States
Hartig, Paul R., Princeton, NJ, United States
PA Synaptic Pharmaceutical Corporation, Paramus, NJ, United States (U.S. corporation)
PI US 5658786 19970819
WO 9318143 19930916
AI US 1994-295814 19941219 (8)
WO 1993-US1959 19930304
19941219 PCT 371 date
19941219 PCT 102(e) date
RLI Continuation-in-part of Ser. No. US 1992-959936, filed on 13 Oct 1992, now abandoned which is a continuation-in-part of Ser. No. US 1992-847742, filed on 4 Mar 1992, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Walsh, Stephen; Assistant Examiner: Kaufman, Claire
LREP White, John P.
CLMN Number of Claims: 13
ECL Exemplary Claim: 1
DRWN 39 Drawing Figure(s); 37 Drawing Page(s)
LN.CNT 3815
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention provides isolated nucleic acid molecules encoding two mammalian GABA transporters, a mammalian taurine transporter and two human GABA transporters and methods of isolating these nucleic acid molecules. Further provided are vectors comprising the nucleic acid molecules as well as mammalian cells comprising such vectors, and antibodies directed to the GABA and taurine transporters. Nucleic acid probes useful for detecting nucleic acid molecules encoding GABA and taurine transporters are also provided. Antisense oligonucleotides complementary to any sequences of a nucleic acid molecule which encodes a GABA or taurine transporter are further provided. Pharmaceutical compounds related to GABA and taurine transporters are provided. Nonhuman transgenic animals which express DNA encoding a normal or a mutant GABA or taurine transporter are also provided. Further provided are methods for determining substrate binding, detecting expression,

drug screening, and treatments for alleviating abnormalities associated with GABA and taurine transporters.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . diazepam and related benzodiazepines has proven extremely useful in the treatment of generalized anxiety (77) and in certain forms of **epilepsy** (57).

SUMM . . . Osmoregulation is essential to normal brain function and may also play a critical role in various pathophysiological states such as **epilepsy**, migraine, and ischemia. The primary mechanism by which neurons and glial cells regulate osmolarity is via the selective accumulation and. . .

DETD . . . composition described above effective to reduce expression of the GABA transporter by the subject. Examples of such abnormal conditions are **epilepsy** and generalized anxiety. This invention also provides a method of treating abnormalities which are alleviated by reduction of expression of. . . composition described above effective to reduce expression of the taurine transporter by the subject. Examples of such abnormal conditions are **epilepsy**, migraine, and ischemia.

DETD . . . the transporter and thereby alleviate the abnormal condition. Some examples of abnormal conditions associated with excess GABA transporter activity are **epilepsy** and generalized anxiety. Excess taurine transporter activity associated disorders are **epilepsy**, migraine, and ischemia.

DETD . . . GABA and taurine transporter structure and function provides a model for the development of drugs useful for the treatment of **epilepsy**, generalized anxiety, migraine, ischemia and other neurological disorders.

DETD . . . a plating density of 15.times.10.sup.6 cells per 100 mm dish was employed; the medium was supplemented with insulin. Cytosine arabinoside (**ara-C**) was added to a final concentration of 10 .mu.M on day 2 or 3 to inhibit the proliferation of non-neuronal. . .

DETD 35. Krnjevic, K. (1991) in GABA Mechanisms in **Epilepsy**, ed. G. Tunnicliff and B. U. Raess, pp 47-87, Wiley-Liss, NY.

DETD 36. Krogsgaard-Larsen, P., Falch, E., Larsson, O. M., and Schousboe, A. (1987) **Epilepsy** Res. 1, 77-93.

DETD 41. Lombardini, J. B. (1988) Effects of taurine and **mitochondrial** metabolic inhibitors on ATP-dependent Ca.sup.2+ uptake in synaptosomal and **mitochondrial** subcellular fractions of rat retina, J. Neurochemistry 51, 200-205.

DETD 62. Schousboe, A., Larsson, O. M., and Krogsgaard-Larsen, P. (1991) in GABA Mechanisms in **Epilepsy**, ed. G. Tunnicliff and B. U. Raess, pp 165-187, Wiley-Liss, NY.

DETD 73. Twyman, R. E. and Macdonald, R. L. (1991) in GABA Mechanisms in **Epilepsy**, editors G. Tunnicliff and B. U. Raess, pp 89-104, Wiley-Liss, NY.

DETD . . . N. M. Neuronal discharge hypersynchrony and the intracranial water balance in relation to glutamic acid and taurine redistribution: Migraine and **epilepsy**. Prog. Clin. Biol. Res. 351:1-20 (1990).

L11 ANSWER 14 OF 14 USPATFULL

AN 93:82731 USPATFULL

TI Diagnostic methods using neurite growth regulatory factors

IN Schwab, Martin E., Zurich, Switzerland
Caroni, Pierenrico W., Zurich, Switzerland
Paganetti, Paolo A., Zurich, Switzerland

PA Erziehungsdirektion of the Canton Zurich, Zurich, Switzerland (non-U.S. corporation)

PI US 5250414 19931005

AI US 1991-719692 19910624 (7)

RLI Continuation-in-part of Ser. No. US 1989-401212, filed on 30 Aug 1989 which is a continuation-in-part of Ser. No. US 1988-267941, filed on 4 Nov 1988, now abandoned

DT Utility

FS Granted

EXNAM Primary Examiner: Hill, Jr., Robert J.; Assistant Examiner: Cermak, Shelly Guest
LREP Pennie & Edmonds
CLMN Number of Claims: 17
ECL Exemplary Claim: 1
DRWN 96 Drawing Figure(s); 41 Drawing Page(s)
LN.CNT 5260
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The proteins of the present invention include central nervous system myelin associated proteins and metalloproteases associated with glioblastoma cells and other malignant tumors which can metastasize to the brain. The CNS myelin associated proteins inhibit neurite outgrowth in nerve cells and neuroblastoma cells, and can also inhibit fibroblast spreading. Such inhibitory proteins include a 35,000 dalton and a 250,000 dalton molecular weight protein. The CNS myelin associated inhibitory proteins may be used in the treatment of malignant tumors. Antibodies to the CNS myelin associated proteins can be used in the diagnosis and therapies of nerve damage. Monoclonal antibody IN-1 may be used to promote regeneration of nerve fibers over long distances in spinal cord lesions. The metalloproteases of the invention have value in diagnosis of malignancies and the treatment of nerve damage and degenerative disorders of the nervous system. Inhibitors of the metalloproteases in combination with the CNS myelin associated inhibitory proteins can be used in the treatment of malignant tumors. Methods of determining malignant potential of a cell by measuring metalloprotease activity are provided.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
DETD . . . to toxic agents, nutritional deficiency, paraneoplastic syndromes, and degenerative nerve diseases (including but not limited to Alzheimer's disease, Parkinson's disease, **Huntington**'s Chorea, amyotrophic lateral sclerosis, progressive supra-nuclear palsy, and other dementias). In a specific embodiment, such molecules may be used to. . .
DETD . . . treated with such inhibitory protein antagonists. Examples of such disorders include but are not limited to Alzheimer's Disease, Parkinsons' Disease, **Huntington**'s Chorea, amyotrophic lateral sclerosis, progressive supranuclear palsy and other dementias. Such antagonists may be used to promote the regeneration of. . .
DETD . . . infarction, or degenerative disorders of the central nervous system which include but are not limited to Alzheimer's disease, Parkinson's disease, **Huntington**'s Chorea, amyotrophic lateral sclerosis, or progressive supranuclear palsy. For example, in one embodiment, CNS myelin associated inhibitory protein receptors, or. . .
DETD . . . 6:3031-3038). In order to suppress the growth of Schwann cells added together with the peripheral neurons, pulses of cytosine arabinoside (**Ara C**, 10.sup.-5 M) were given twice for 24 hours on the 2nd and 5th day of co-culture in some experiments. The. . .
DETD . . . were added to glial cells after 2-10 days in culture. Ganglionic Schwann cells and fibroblasts were eliminated by pulses of **Ara C** in some of the experiments. NGF (50 or 100 ng/ml) was added to the culture medium, leading to a rapid. . .
DETD . . . 7.4 (Quigley, 1976, J. Cell Biol. 71: 472-486). 20-40% sucrose interphase (C6 plasma membranes fraction) and 40-60% sucrose interphase (C6 **mitochondrial** fraction) were collected, washed in Hank's medium and resuspended in MEM.
DETD . . . centrifuged at 80,000.times.g for 1 h in a Beckman SW28 motor. Plasma membranes were harvested at the top and the **mitochondrial** fraction at the interphase of this 2 step gradient. Both fractions were diluted 10.times. with CMF-Hank's and pelleted (Beckman TI80,. . .
DETD . . . fractions. Maximal activity was associated with the plasma membrane (2.7 nMol/min). On the other hand, crude homogenate (0.08 nMol/min) and **mitochondrial** fraction (0.27 nMol/min) were clearly less active. No activity was found in C6 cell conditioned medium (0.03 nMol/min (FIG. 30a).. . .

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=> s l4 or l5 or l6
L12       48804 L4 OR L5 OR L6

=> s l7 and l12
  29 FILES SEARCHED...
L13         344 L7 AND L12
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L14 ANSWER 72 OF 84 USPATFULL
AN 1999:18977 USPATFULL
TI **Mitochondrial** processing peptidase subunit
IN Bandman, Olga, Mountain View, CA, United States
Shah, Purvi, Sunnyvale, CA, United States
Corley, Neil C., Mountain View, CA, United States
PA Incyte Pharmaceuticals, Inc., Palo Alto, CA, United States (U.S. corporation)
PI US 5869311 19990209
AI US 1997-895521 19970717 (8)
DT Utility
FS Granted
EXNAM Primary Examiner: Hendricks, Keith D.; Assistant Examiner: Mayhew, Bradley S.
LREP Incyte Pharmaceuticals, Inc., Billings, Lucy J., Mohan-Peterson, Sheela
CLMN Number of Claims: 10
ECL Exemplary Claim: 1
DRWN 11 Drawing Figure(s); 11 Drawing Page(s)
LN.CNT 2291
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention provides a human **mitochondrial** processing peptidase subunit (MPPS-1) and polynucleotides which identify and encode MPPS-1. The invention also provides expression vectors, host cells, agonists, antibodies and antagonists. The invention also provides methods for treating disorders associated with expression of MPPS-1.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
TI **Mitochondrial** processing peptidase subunit
AB The invention provides a human **mitochondrial** processing peptidase subunit (MPPS-1) and polynucleotides which identify and encode MPPS-1. The invention also provides expression vectors, host cells, agonists,. . .
SUMM This invention relates to nucleic acid and amino acid sequences of a **mitochondrial** processing peptidase subunit and to the use of these sequences in the diagnosis, prevention, and treatment of smooth muscle disorders,. . .
SUMM **Mitochondria** are the primary sites of energy production in cells. Energy production occurs through the action of a series of enzyme complexes called the **mitochondrial** electron transport (or respiratory) chain. These complexes are responsible for: 1) the transport of electrons from NADH to oxygen and,. . .
SUMM Most **mitochondrial** proteins are the products of nuclear genes and are imported into the **mitochondria** from the cytosol following their synthesis. Targeting of these proteins to **mitochondria** is achieved by an N-terminal leader (or signal) peptide of 10 to 70 amino acid residues which contains many positively charged amino acids. Once these precursor proteins are localized in the **mitochondria**, the leader peptide is cleaved by a signal peptidase to generate the mature protein. Most leader peptides are removed in a one step process by a protease termed **mitochondrial** processing peptidase (MPP) (Paces, V. et al. (1993) Proc. Natl. Acad. Sci. 90:5355-58). In some cases a two-step process occurs in which MPP generates an intermediate precursor form which is cleaved by a second enzyme, **mitochondrial** intermediate peptidase, to generate the mature protein.
SUMM . . . has a predicted signal peptidase cleavage site sequence, RST.sub.45 QA. Paces et al.(supra) suggest that, after being imported into the **mitochondria**, beta-MPP is cleaved by pre-existing MPP. An alpha-helical structure is predicted in the region between amino acids 165 and 205. . .
SUMM The discovery of a new **mitochondrial** processing peptidase subunit and the polynucleotides encoding it satisfies a need in the art by providing new compositions which are. . .
SUMM The invention features a substantially purified polypeptide, **mitochondrial** processing peptidase subunit (MPPS-1), having the amino acid sequence shown in SEQ ID NO:1, or fragments thereof.

DRWD FIGS. 2A, 2B, and 2C show the amino acid sequence alignments among MPPS-1 (457485; SEQ ID NO:1), the beta-subunit of **mitochondrial** processing peptidase from rat, beta-MPP (GI 294589; SEQ ID NO:3) and human ubiquinol-cytochrome-c reductase, core I protein (GI 1082896; SEQ. . .

DETD The invention is based on the discovery of a new human **mitochondrial** processing peptidase subunit (hereinafter referred to as "MPPS-1"), the polynucleotides encoding MPPS-1, and the use of these compositions for the. . .

DETD . . . bridging sites are found at C.sub.62, C.sub.79, C.sub.265, C.sub.277, C.sub.312, C.sub.369, C.sub.428, and C.sub.454. Residues M.sub.1 -T.sub.45 represent a potential **mitochondrial** signal peptide with seven positively charged arginine residues and a predicted signal peptidase cleavage site sequence at RST.sub.45 QA. The. . .

DETD Chemical and structural homology exists between/among MPPS-1, the beta-subunit of **mitochondrial** processing peptidase from rat (GI 294589; SEQ ID NO:3), and human ubiquinol-cytochrome-c reductase, core I protein (GI 1082896; SEQ ID. . .

DETD . . . anaphylactic shock, arrhythmias, asthma, cardiovascular shock, Cushing's syndrome, hypertension, hypoglycemia, myocardial infarction, migraine, and pheochromocytoma, and myopathies including cardiomyopathy, encephalopathy, **epilepsy**, Kearns-Sayre syndrome, lactic acidosis, myoclonic disorder, and ophthalmoplegia. Smooth muscle includes, but is not limited to, that of the blood. . .

DETD . . . to, akathesia, Alzheimer's disease, amnesia, amyotrophic lateral sclerosis, bipolar disorder, catatonia, cerebral neoplasms, dementia, depression, Down's syndrome, tardive dyskinesia, dystonias, **epilepsy**, **Huntington**'s disease, multiple sclerosis, neurofibromatosis, Parkinson's disease, paranoid psychoses, schizophrenia, and Tourette's disorder.

DETD . . . nontraditional bases such as inosine, queosine, and wybutosine, as well as acetyl-, methyl-, thio-, and similarly modified forms of adenine, **cytidine**, guanine, thymine, and uridine which are not as easily recognized by endogenous endonucleases.

DETD . . . anaphylactic shock, arrhythmias, asthma, cardiovascular shock, Cushing's syndrome, hypertension, hypoglycemia, myocardial infarction, migraine, and pheochromocytoma, and myopathies including cardiomyopathy, encephalopathy, **epilepsy**, Kearns-Sayre syndrome, lactic acidosis, myoclonic disorder, and ophthalmoplegia; neurological disorders such as akathesia, Alzheimer's disease, amnesia, amyotrophic lateral sclerosis, bipolar disorder, catatonia, cerebral neoplasms, dementia, depression, Down's syndrome, tardive dyskinesia, dystonias, **epilepsy**, **Huntington**'s disease, multiple sclerosis, neurofibromatosis, Parkinson's disease, paranoid psychoses, schizophrenia, and Tourette's disorder; and cancer such as adenocarcinoma, leukemia, lymphoma, melanoma,. . .

DETD . . . astrocytoma localized in the left frontal part of the brain. Prior to surgery the patient was also diagnosed with coma, **epilepsy**, and paralysis. The patient's history included a diagnosis of chronic nephritis.

DETD MPPS-1 activity is measured in reconstituted MPP by the hydrolysis of a signal peptide from a **mitochondrial** protein precursor (Kleiber, J. et al. (1990) Proc. Natl. Acad. Sci. 87:7978-82). MPPS-1 is first reconsituted with alpha-MPP to form. . .

CLM What is claimed is:

9. A method for detecting a polynucleotide which encodes a **mitochondrial** processing peptidase subunit in a biological sample comprising the steps of: a) hybridizing the polynucleotide of claim 3 to nucleic. . . b) detecting said hybridization complex, wherein the presence of said complex correlates with the presence of a polynucleotide encoding the **mitochondrial** processing peptidase subunit in said biological sample.

L14 ANSWER 73 OF 84 USPATFULL

AN 1999:4379 USPATFULL

TI Human metaxin protein

IN Hillman, Jennifer L., Mountain View, CA, United States
Corley, Neil C., Mountain View, CA, United States
Shah, Purvi, Sunnyvale, CA, United States
PA Incyte Pharmaceuticals, Inc., Palo Alto, CA, United States (U.S. corporation)
PI US 5858714 19990112
AI US 1997-864799 19970529 (8)
DT Utility
FS Granted
EXNAM Primary Examiner: Wax, Robert A.; Assistant Examiner: Longton, Enrique D.
LREP Incyte Pharmaceuticals, Inc., Billings, Lucy J., Muenzen, Colette C.
CLMN Number of Claims: 11
ECL Exemplary Claim: 1
DRWN 11 Drawing Figure(s); 11 Drawing Page(s)
LN.CNT 2234
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention provides a human metaxin protein and polynucleotides which identify and encode MTXP-1. The invention also provides expression vectors, host cells, agonists, antibodies and antagonists. The invention also provides methods for treating disorders associated with expression of MTXP-1.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUMM . . . and human. It is characterized by relatively high levels (10-15%) of leucine, and acidic and basic residues. MTX is a **mitochondrial** protein encoded by a nuclear gene, but does not contain an amino-terminal signal sequence or N-glycosylation sites. A putative hydrophobic. . .
DETD . . . system, reproductive system, etc. Such disorders include, but are not limited to, renal tubular acidosis, anemia, Cushing's syndrome, achondroplastic dwarfism, **epilepsy**, gonadal dysgenesis, hereditary neuropathies such as Charcot-Marie-Tooth disease and neurofibromatosis, hypothyroidism, hydrocephalus, seizure disorders such as Syndenham's chorea and cerebral. . .
DETD . . . nontraditional bases such as inosine, queosine, and wybutosine, as well as acetyl-, methyl-, thio-, and similarly modified forms of adenine, **cytidine**, guanine, thymine, and uridine which are not as easily recognized by endogenous endonucleases.
DETD . . . MTXP-1. Examples of such conditions or diseases include developmental disorders such as renal tubular acidosis, anemia, Cushing's syndrome, achondroplastic dwarfism, **epilepsy**, gonadal dysgenesis, hereditary neuropathies such as Charcot-Marie-Tooth disease and neurofibromatosis, hypothyroidism, hydrocephalus, seizure disorders such as Syndenham's chorea and cerebral. . .

L14 ANSWER 74 OF 84 USPATFULL
AN 1999:1498 USPATFULL
TI **Mitochondrial** adenylate kinase
IN Hillman, Jennifer L., San Jose, CA, United States
Shah, Purvi, Sunnyvale, CA, United States
PA Incyte Pharmaceuticals, Inc., Palo Alto, CA, United States (U.S. corporation)
PI US 5856160 19990105
AI US 1997-829027 19970331 (8)
DT Utility
FS Granted
EXNAM Primary Examiner: Lau, Kawai
LREP Billings, Lucy J., Mohan-Peterson, SheelaIncyte Pharmaceuticals, Inc.
CLMN Number of Claims: 9
ECL Exemplary Claim: 1
DRWN 10 Drawing Figure(s); 10 Drawing Page(s)
LN.CNT 2007
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides a human **mitochondrial** adenylate kinase (HMAK) and polynucleotides which encode HMAK. The invention also provides expression vectors, host cells, agonists, antisense molecules,

antibodies, or antagonists. The invention also provides methods for treating disorders associated with expression of HMAK.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

TI **Mitochondrial** adenylate kinase

AB The present invention provides a human **mitochondrial** adenylate kinase (HMAK) and polynucleotides which encode HMAK. The invention also provides expression vectors, host cells, agonists, antisense molecules, antibodies,. . .

SUMM This invention relates to nucleic acid and amino acid sequences of a novel **mitochondrial** adenylate kinase and to the use of these sequences in the diagnosis, prevention, and treatment of cancer, neurological disorders, and. . .

SUMM . . . al., supra). AK1 is a cytosolic enzyme present in skeletal muscle, brain, and erythrocytes, and AK2 is associated with the **mitochondrial** membrane in liver, kidney, spleen, and heart. Both AK1 and AK2 use ATP as the phosphate donor substrate. AK3 is also a **mitochondrial** enzyme, primarily found in liver and heart, but uses GTP as the phosphate donor. AK2 and AK3 are unusual in that they do not have a cleavable N-terminal sequence directing them to the **mitochondrial** membrane as do most **mitochondrial** proteins (Yamada et al., supra). Targeting of these proteins to the **mitochondria** appears to be governed by a non-cleavable N-terminal sequence that contains a positively charged amphipathic region. This targeting sequence also. . .

SUMM The discovery of polynucleotides encoding a novel **mitochondrial** adenylate kinase and the molecules themselves satisfies a need in the art by providing new diagnostic or therapeutic compositions useful. . .

SUMM The present invention features a novel human **mitochondrial** adenylate kinase hereinafter designated HMAK and characterized as having similarity to other microsomal signal peptidase subunits.

SUMM . . . associated with expression of HMAK by administration of HMAK or antagonists of HMAK, and methods for detection of polynucleotides encoding **mitochondrial** adenylate kinase in a biological sample.

DETD . . . structure of HMAK or portions thereof and, as such, is able to effect some or all of the actions of **mitochondrial** adenylate kinase-like molecules.

DETD The invention is based on the discovery of a novel human **mitochondrial** adenylate kinase, (HMAK), the polynucleotides encoding IIMAK, and the use of these compositions for the diagnosis, prevention, or treatment of. . .

DETD . . . between residues R6 and V23 constitutes a positively charged, amphipathic region that may be important for targeting HMAK to the **mitochondrial** membrane. Positively charged residues at R6, R9, and K20 are known to be important for this function and are shared. . .

DETD . . . administered to a subject to treat a neurological disorder. Neurological disorders may include, but are not limited to, Alzheimer's disease, **Huntington**'s disease, Parkinson's disease, **epilepsy**, Down's syndrome, dementia, multiple sclerosis, neurofibromatosis, and amyotrophic lateral sclerosis.

DETD . . . nontraditional bases such as inosine, qucosine, and wybutosine, as well as acetyl-, methyl-, thio-, and similarly modified forms of adenine, **cytidine**, guanine, thymine, and uridine which are not as easily recognized by endogenous endonucleases.

DETD . . . which are associated with expression of HMAK. Examples of such conditions or diseases include neurological disorders such as Alzheimer's disease, **Huntington**'s disease, Parkinson's disease, **epilepsy**, Down's syndrome, dementia, multiple sclerosis, neurofibromatosis, and amyotrophic lateral sclerosis; cancers of the skeletal muscle, colon, liver, spleen, breast, skin,. . .

CLM What is claimed is:

9. A method for detection of a polynucleotide encoding a **mitochondrial** adenylate kinase in a biological sample comprising the steps of: a) hybridizing the polynucleotide of claim 6 to nucleic

acid. . . b) detecting said hybridization complex, wherein the presence of said complex correlates with the presence of a polynucleotide encoding a **mitochondrial** adenylate kinase in said biological sample.

L14 ANSWER 75 OF 84 USPATFULL
AN 1998:157139 USPATFULL
TI Polynucleotides encoding ATP synthase coupling factor 6
IN Hillman, Jennifer L., Mountain View, CA, United States
Shah, Purvi, Sunnyvale, CA, United States
PA Incyte Phamaceuticals, Inc., Palo Alto, CA, United States (U.S. corporation)
PI US 5849527 19981215
AI US 1997-828239 19970331 (8)
DT Utility
FS Granted
EXNAM Primary Examiner: Spector, Lorraine; Assistant Examiner: Romeo, David S.
LREP Incyte Pharmaceuticals, Inc.
CLMN Number of Claims: 9
ECL Exemplary Claim: 1
DRWN 7 Drawing Figure(s); 7 Drawing Page(s)
LN.CNT 1950
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides a human **mitochondrial** F6 subunit (HMF6) and polynucleotides which encode HMF6. The invention also provides expression vectors, host cells, agonists, antisense molecules, antibodies, or antagonists. The invention also provides methods for treating disorders associated with expression of HMF6.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides a human **mitochondrial** F6 subunit (HMF6) and polynucleotides which encode HMF6. The invention also provides expression vectors, host cells, agonists, antisense molecules, antibodies,. . .
SUMM The **mitochondrial** electron transport (or respiratory) chain is a series of enzyme complexes in the **mitochondrial** membrane that is responsible for the transport of electrons from NADH to oxygen and the coupling of this oxidation to. . .
SUMM . . . this chain and serves as a reversible coupling device that interconverts the energies of an electrochemical proton gradient across the **mitochondrial** membrane into either the synthesis or hydrolysis of ATP. This gradient is produced by other enzymes of the respiratory chain. . . oxygen. When the cell's energy demands are high, electron transport from NADH to oxygen generates an electrochemical gradient across the **mitochondrial** membrane. Proton translocation from the outer to the inner side of the membrane drives the synthesis of ATP. Under conditions. . . gradient is reversed and ATP synthase hydrolyzes ATP. The energy of hydrolysis is used to pump protons out of the **mitochondrial** matrix.
SUMM . . . pump, and F.sub.1 is the catalytic portion that synthesizes or hydrolyzes ATP. The mammalian ATP synthase complex from bovine heart **mitochondria** consists of sixteen different polypeptides (Walker, J. E. and Collinson, T. R. (1994) FEBS Lett.346: 39-43). Six of these polypeptides. . . and an ATPase inhibitor protein, IF.sub.1) comprise the globular catalytic F.sub.1 portion of the complex, which lies outside of the **mitochondrial** membrane. The remaining ten polypeptides (subunits a, b, c, d, e, f, g, F6, OSCP, and A6L) comprise the proton-translocating,. . .
SUMM . . . for the oligomycin-sensitive ATPase activity in the complex. F6 is a small 76 amino acid coupling factor that, like most **mitochondrial** proteins, is the product of a nuclear gene that is imported into the **mitochondria**. F6 is synthesized as a 108 amino acid precursor; the N-terminal 32 amino acids constitute an import signal peptide that targets the protein to the **mitochondrial** membrane (Higuti, T. et al. (1990) Biochem. Biophys. Res. Commun. 171(3):1079-86). Similar import sequences are found in the F6 precursor.

. . an amphipathic .alpha.-helical region with opposing positively charged and hydrophobic faces that are important for transporting the protein through the **mitochondrial** inner membrane (Higuti et al. (1990), supra).

SUMM The discovery of polynucleotides encoding a human **mitochondrial** F6 subunit and the molecules themselves provides a means to investigate the control of cellular respiration under normal and disease. . .

SUMM The present invention features a novel human **mitochondrial** F6 subunit hereinafter designated HMF6 and characterized as having similarity to other **mitochondrial** F6 subunits.

SUMM . . . associated with expression of HMF6 by administration of HMF6 or antagonists of HMF6, and methods for detection of polynucleotides encoding **mitochondrial** F6 in a biological sample.

DETD . . . structure of HMF6 or portions thereof and, as such, is able to effect some or all of the actions of **mitochondrial** F6-like molecules.

DETD The invention is based on the discovery of a novel human **mitochondrial** F6 subunit, (HMF6), the polynucleotides encoding HMF6, and the use of these compositions for the diagnosis, prevention, or treatment of. . .

DETD . . . regions between M1 and F32 in F6 from human, cow, and rat. These terminal sequences have been identified as the **mitochondrial** import sequence for these proteins. In particular, positively charged residues at M7, R11, R14, and R20 and the hydrophobic residues. . .

DETD . . . a subject to treat a myopathy. Myopathies may include, but are not limited to, progressive external ophthalmoplegia, Kearns-Sayre syndrome, myoclonic **epilepsy**, encephalopathy, cardiomyopathy, and lactic acidosis.

DETD . . . be administered to a subject to treat a neurodegenerative disease. Diseases may include, but are not limited to, Alzheimer's disease, **Huntington**'s disease, Parkinson's disease, **epilepsy**, Down's syndrome, dementia, multiple sclerosis, neurofibromatosis, and amyotrophic lateral sclerosis.

DETD . . . nontraditional bases such as inosine, queosine, and wybutosine, as well as acetyl-, methyl-, thio-, and similarly modified forms of adenine, **cytidine**, guanine, thymine, and uridine which are not as easily recognized by endogenous endonucleases.

DETD . . . with expression of HMF6. Examples of such conditions or diseases include myopathies such as progressive external ophthalmoplegia, Kearns-Sayre syndrome, myoclonic **epilepsy**, encephalopathy, cardiomyopathy, and lactic acidosis; neurodegenerative diseases such as Alzheimer's disease, **Huntington**'s disease, Parkinson's disease, **epilepsy**, Down's syndrome, dementia, multiple sclerosis, neurofibromatosis, and amyotrophic lateral sclerosis; and cancers of the heart, brain, ovaries, parathyroid, breast, colon,. . .

DETD . . . is combined with F.sub.1 ATPase to form a functional ATP synthase. Bovine submitochondrial particles are prepared by sonication of intact **mitochondria** and isolated from the preparation by differential centrifugation. The assay is performed by incubating the reconstituted ATP synthase, submitochondrial particles,. . .

L14 ANSWER 76 OF 84 USPATFULL

AN 1998:138682 USPATFULL

TI Polynucleotides encoding a cofactor A-like protein

IN Hillman, Jennifer L., San Jose, CA, United States
Goli, Surya K., Sunnyvale, CA, United States

PA Incyte Pharmaceuticals, Inc., Palo Alto, CA, United States (U.S. corporation)

PI US 5834239 19981110

AI US 1997-825782 19970408 (8)

DT Utility

FS Granted

EXNAM Primary Examiner: Kemmerer, Elizabeth C.; Assistant Examiner: Romeo, David S.

LREP Mohan-Peterson, Sheela, Billings, Lucy J.Incyte Pharmaceuticals, Inc.

CLMN Number of Claims: 9
ECL Exemplary Claim: 1
DRWN 3 Drawing Figure(s); 3 Drawing Page(s)
LN.CNT 1933
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides a human cofactor A-like protein (COAPR) and polynucleotides which identify and encode COAPR. The invention also provides expression vectors, host cells, agonists, antibodies and antagonists. The invention also provides methods for treating disorders associated with expression of COAPR.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUMM . . . The first class of chaperones, exemplified by the heat shock protein, hsp70, is found in the cytosol, endoplamic reticulum, and **mitochondria**, and binds to proteins that are unfolded or partially unfolded. Binding prevents protein aggregation and is maintained until the protein. . .
DETD . . . treat or prevent disorders associated with protein folding and assembly. Types of disorders may include, but are not limited to, **epilepsy**, Alzheimer's disease, chronic wound healing, cytotoxic drug resistance, rheumatoid arthritis, scleroderma, male sterility; and disorders of chromosomal disjunction and translocation. . .
DETD . . . nontraditional bases such as inosine, queosine, and wybutosine, as well as acetyl-, methyl-, thio-, and similarly modified forms of adenine, **cytidine**, guanine, thymine, and uridine which are not as easily recognized by endogenous endonucleases.
DETD . . . and particularly, cancers of the breast, ovary, prostate, testicle, stomach, colon, pancreas, bladder, liver, kidney, adrenals, lung, heart, and brain; **epilepsy**, Alzheimer's disease, chronic wound healing, cytotoxic drug resistance, rheumatoid arthritis, scleroderma, male sterility; and disorders of chromosomal disjunction and translocation. . .

L14 ANSWER 77 OF 84 USPATFULL
AN 1998:135161 USPATFULL
TI Human cytochrome B5
IN Hillman, Jennifer L., San Jose, CA, United States
Goli, Surya K., Sunnyvale, CA, United States
Streeter, David Gray, Boulder Creek, CA, United States
PA Incyte Pharmaceuticals, Inc., Palo Alto, CA, United States (U.S. corporation)
PI US 5831018 19981103
AI US 1997-801972 19970218 (8)
DT Utility
FS Granted
EXNAM Primary Examiner: Jacobson, Dian C.; Assistant Examiner: Moore, William W.
LREP Billings, Lucy J., Mohan-Peterson, SheelaIncyte Pharmaceuticals, Inc.
CLMN Number of Claims: 8
ECL Exemplary Claim: 1
DRWN 6 Drawing Figure(s); 4 Drawing Page(s)
LN.CNT 1971
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides a human cytochrome b5 (HCB5) and polynucleotides which encode HCB5. The invention also provides genetically engineered expression vectors and host cells and a method for producing HCB5. The invention also provides for agonists, antisense molecules, antibodies, or antagonists of HCB5, and their use in the prevention and treatment of diseases associated with expression of HCB5. The invention also provides a method for detecting polynucleotides which encode HCB5.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUMM . . . These classifications are not functionally important. Cytochromes a, a.sub.3, b.sub.562, b.sub.566, c, and c.sub.1 are all components of the mammalian **mitochondrial** membrane respiratory chain involved in oxidative phosphorylation. Cyt b5 exists in both a

membrane-bound form found in **mitochondria** and endoplasmic reticulum and a soluble form found in erythrocytes. The membrane-bound form has been linked with lipid and drug. . . approximately residue 96 to the end of the molecule, is a membrane-binding domain that anchors the polypeptide chain to the **mitochondrial** membrane. Studies with the rat cytochrome b5 also indicate that the targeting information for directing this protein to the **mitochondrial** membrane resides in the C-terminal sequence rather than in an N-terminal signal sequence as is common in other **mitochondrial** proteins (De Silvestris, et al., supra). Since the rat protein also lacks the N-terminal 30 amino acids found in most other **mitochondrial** isoforms, the catalytic region of these proteins is further defined as existing between residues 30 to 96. The soluble form. . .

DETD . . . treat or prevent a myopathy. Such myopathies may include, but are not limited to, progressive external ophthalmoplegia, Kearns-Sayre syndrome, myoclonic **epilepsy**, encephalopathy, cardiomyopathy, and lactic acidosis.

DETD . . . nontraditional bases such as inosine, queosine, and wybutosine, as well as acetyl-, methyl-, thio-, and similarly modified forms of adenine, **cytidine**, guanine, thymine, and uridine which are not as easily recognized by endogenous endonucleases.

DETD . . . of such conditions or diseases include, but are not limited to, myopathies such as progressive external ophthalmoplegia, Kearns-Sayre syndrome, myoclonic **epilepsy**, encephalopathy, cardiomyopathy, and lactic acidosis; growth and development disorders such as hypothyroidism, achondroplastic dwarfism, renal tubular acidosis, anemia, and gonadal. . .

L14 ANSWER 78 OF 84 USPATFULL

AN 1998:131587 USPATFULL

TI Succinate-ubiquinone reductase subunit

IN Lal, Preeti, Sunnyvale, CA, United States
Shah, Purvi, Sunnyvale, CA, United States

PA Incyte Pharmaceuticals, Inc., Palo Alto, CA, United States (U.S. corporation)

PI US 5827711 19981027

AI US 1997-828832 19970320 (8)

DT Utility

FS Granted

EXNAM Primary Examiner: Hendricks, Keith D.; Assistant Examiner: Mayhew, Bradley S.

LREP Billings, Lucy J., Mohan-Peterson, SheelaIncyte Pharmaceuticals, Inc.

CLMN Number of Claims: 8

ECL Exemplary Claim: 1

DRWN 6 Drawing Figure(s); 6 Drawing Page(s)

LN.CNT 1991

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention provides a human succinate-ubiquinone reductase membrane anchor subunit (SDHMA) and polynucleotides which encode SDHMA. The invention also provides expression vectors, host cells, agonists, antisense molecules, antibodies, or antagonists. The invention also provides methods for treating disorders associated with expression of SDHMA.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM The **mitochondrial** electron transport (or respiratory) chain is a series of enzyme complexes in the **mitochondrial** membrane that is responsible for the transport of electrons from NADH through a series of redox centers within these complexes. . .

SUMM . . . (complex IV), and ATP synthase (complex V). All of these complexes are located on the inner matrix side of the **mitochondrial** membrane except complex II, which is on the cytosolic side. Complex II transports electrons generated in the citric acid cycle. . .

SUMM Complex II from bovine heart **mitochondria** is composed of two fractions. The soluble succinate dehydrogenase (SDH) fraction catalyzes the oxidation of succinate to fumarate. In addition. . . a series of

iron-sulfur clusters which serve as electron transport centers. The membrane anchoring fraction, QPs, binds SDH to the **mitochondrial** membrane and provides the link between SDH and Q (Lee, G. Y. et al. (1995) J. Biol. Chem. 270(11):6193-98). In. . .

SUMM . . . other proteins in the respiratory chain, the subunits of complex II are nuclear gene products and are imported into the **mitochondria**. Signal sequences that target these proteins to the **mitochondria** have been determined for subunits in both the catalytic and membrane anchoring fractions (Birch-Machin, M. A. et al., (1992) J.. . .

DRWD . . . 2 shows the amino acid sequence alignments among SDHMA (SEQ ID NO:1), and the membrane anchoring proteins from bovine heart **mitochondria**, QPs3 (GI 1575011; SEQ ID NO:3), and QPs1 (GI 1705529; SEQ ID NO:4). The alignment was produced using the multisequence. . .

DETD . . . and C150. As shown in FIG. 2, SDHMA has chemical and structural homology with the membrane anchoring subunits from bovine **mitochondria**, QPs3 (GI 599873; SEQ ID NO:3) and QPs1 (GI 220904; SEQ ID NO:4). In particular, SDHMA shares 87% and 21%. . . The N-terminal 28-30 amino acids of SDHMA, Qps1, and QPs3 represents a potential signal sequence for targeting SDHMA to the **mitochondria**. As illustrated by FIGS. 3A, 3B, and 3C, SDHMA, Qps3, and Qps1 have rather similar hydrophobicity plots. In particular, prominent. . .

DETD . . . a subject to treat a myopathy. Myopathies may include, but are not limited to, progressive external ophthalmoplegia, Kearns-Sayre syndrome, myoclonic **epilepsy**, encephalopathy, cardiomyopathy, and lactic acidosis.

DETD . . . nontraditional bases such as inosine, queosine, and wybutosine, as well as acetyl-, methyl-, thio-, and similarly modified forms of adenine, **cytidine**, guanine, thymine, and uridine which are not as easily recognized by endogenous endonucleases.

DETD . . . with expression of SDHMA. Examples of such conditions or diseases include myopathies such as progressive external ophthalmoplegia, Kearns-Sayre syndrome, myoclonic **epilepsy**, encephalopathy, cardiomyopathy, and lactic acidosis; cancers of the heart, blood, pancreas, eye, colon, skin, liver, breast, ovaries, spleen, bone, muscle,. . .

L14 ANSWER 79 OF 84 USPATFULL

AN 1998:122238 USPATFULL

TI Disease related nucleotide kinases

IN Bandman, Olga, Mountain View, CA, United States
Hillman, Jennifer L., Mountain View, CA, United States
Hawkins, Phillip R., Mountain View, CA, United States
Guegler, Karl J., Menlo Park, CA, United States
Corley, Neil C., Mountain View, CA, United States

PA Incyte Pharmaceuticals, Inc., Palo Alto, CA, United States (U.S. corporation)

PI US 5817482 19981006

AI US 1997-879561 19970620 (8)

DT Utility

FS Granted

EXNAM Primary Examiner: Wax, Robert A.; Assistant Examiner: Longton, Enrique D.

LREP Mohan-Peterson, Sheela, Billings, Lucy J.Incyte Pharmaceuticals, Inc.

CLMN Number of Claims: 11

ECL Exemplary Claim: 1

DRWN 19 Drawing Figure(s); 19 Drawing Page(s)

LN.CNT 2836

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention provides human nucleotide kinases and polynucleotides which identify and encode DRNK. The invention also provides expression vectors, host cells, agonists, antibodies and antagonists. The invention also provides methods for treating disorders associated with expression of DRNK.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . having high rates of ATP synthesis and utilization such as skeletal muscle. In these cells, AK is physically associated with **mitochondria** and myofibrils, the subcellular structures that are involved in energy production and utilization, respectively. AK catalyzes the reversible transfer of. . . AK1 is present in the cytosol of skeletal muscle, brain, and erythrocytes. AK2 is found in the intermembrane space of **mitochondria** of liver, kidney, and heart. AK3 is found in the **mitochondrial** matrix of liver and heart and uses GTP as the phosphate donor.

DETD . . . is found at G.sub.8, and a potential N-glycosylation site is located at N.sub.141 .The N-terminal 25 amino acids constitute a **mitochondrial** localization signal with important basic residues located within it at K.sub.3, R.sub.13, R.sub.19, R.sub.22, and R.sub.23. As shown in FIG.. . . dGK and dCK, respectively. dGk and dCK both share the ATP/GTP-binding motif (p-loop) found in DRNK-1, and dGK shares the **mitochondrial** localization signal and the potential N-myristoylation and N-glycosylation sites found in DRNK-1. Northern analysis shows the expression of this sequence. . .

DETD . . . to, akathesia, Alzheimer's disease, amnesia, amyotrophic lateral sclerosis, bipolar disorder, catatonia, cerebral neoplasms, dementia, depression, Down's syndrome, tardive dyskinesia, dystonias, **epilepsy**, **Huntington**'s disease, multiple sclerosis, neurofibromatosis, Parkinson's disease, paranoid psychoses, schizophrenia, and Tourette's disorder.

DETD . . . nontraditional bases such as inosine, queosine, and wybutosine, as well as acetyl-, methyl-, thio-, and similarly modified forms of adenine, **cytidine**, guanine, thymine, and uridine which are not as easily recognized by endogenous endonucleases.

DETD . . . as akathesia, Alzheimer's disease, amnesia, amyotrophic lateral sclerosis, bipolar disorder, catatonia, cerebral neoplasms, dementia, depression, Down's syndrome, tardive dyskinesia, dystonias, **epilepsy**, **Huntington**'s disease, multiple sclerosis, neurofibromatosis, Parkinson's disease, paranoid psychoses, schizophrenia, and Tourette's disorder. The polynucleotide sequences encoding DRNK may be used. . .

L14 ANSWER 80 OF 84 USPATFULL

AN 1998:118973 USPATFULL

TI Subunits of NADH dehydrogenase

IN Bandman, Olga, Mountain View, CA, United States
Goli, Surya K., Sunnyvale, CA, United States
Hillman, Jennifer L., San Jose, CA, United States

PA Incyte Pharmaceuticals, Inc., Palo Alto, CA, United States (U.S. corporation)

PI US 5814451 19980929

AI US 1997-785065 19970117 (8)

DT Utility

FS Granted

EXNAM Primary Examiner: Patterson, Jr., Charles L.

LREP Billings, Lucy J.

CLMN Number of Claims: 10

ECL Exemplary Claim: 1

DRWN 21 Drawing Figure(s); 17 Drawing Page(s)

LN.CNT 2382

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention provides four NADH dehydrogenase subunits (designated individually as NDS-1, NDS-2, NDS-3, and NDS-4 and collectively as NDS) and polynucleotides which identify and encode NDS. The invention also provides genetically engineered expression vectors and host cells comprising the nucleic acid sequences encoding NDS and a method for producing NDS. The invention also provides for use of NDS and agonists, antibodies, or antagonists specifically binding NDS, in the prevention and treatment of diseases associated with expression of NDS. Additionally, the invention provides for the use of antisense molecules to polynucleotides encoding NDS for the treatment of diseases associated with the expression of NDS. The invention also provides diagnostic

assays which utilize the polynucleotide, or fragments or the complement thereof, and antibodies specifically binding NDS.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . (NADH:ubiquinone oxidoreductase, NADH-D) is the first multienzyme complex (Complex I) in a chain of three complexes that make up the **mitochondrial** electron transport chain. The **mitochondrial** electron transport chain is responsible for the transport of electrons from NADH to oxygen and the coupling of this oxidation. . .

SUMM NADH-D and the other members of the electron transport chain are located in the **mitochondrial** membrane. NADH-D is the largest of the three complexes with an estimated mass of 800 kDa comprising some 40 polypeptides. . . M. W. J. and Ragan, C. I. (1985) Biochem. J. 230: 739-46). The best characterized NADH-D is from bovine heart **mitochondria** and is composed of 41 polypeptide chains (Walker, J. E. et al. (1992) J. Mol. Biol. 226: 1051-72). Seven of these polypeptides are encoded by **mitochondrial** DNA while the remaining 34 are nuclear gene products that are imported into the **mitochondria**. These imported polypeptides are characterized by various N-terminal peptide sequences or modified N-terminal amino acids (myristoylation or acetylation) that target them to the **mitochondria** and are then cleaved from the mature protein. The 24-, 51-, and 75-kDa subunits have been identified as being catalytically. . .

DETD . . . in the bovine 30-kDa subunit that extends from residues M1 to R37 and serves to direct the protein to the **mitochondria** is well conserved in NDS-1. The sequence is cleaved in the mature protein following the translocation process. In particular, a. . .

DETD . . . tissues of the sympathetic nervous system (paraganglion and smooth muscle tissues), NDS-2 is believed to play a role in cancers, **mitochondrial** myopathies, and disorders of the sympathetic nervous system.

DETD . . . in one embodiment, NDS-2 or a fragment or derivative thereof may be administered to a subject to treat or prevent **mitochondrial** myopathies. Such conditions and diseases may include, but are not limited to, progressive external ophthalmoplegia, Kearns-Sayre syndrome, myoclonic **epilepsy**, encephalopathy, cardiomyopathy, and lactic acidosis.

DETD . . . NDS-2, or a fragment or a derivative thereof, may also be administered to a subject to treat or prevent the **mitochondrial** myopathies listed above.

DETD . . . in one embodiment, NDS-3 or a fragment or derivative thereof may be administered to a subject to treat or prevent **mitochondrial** myopathies. Such conditions and diseases may include, but are not limited to, progressive external ophthalmoplegia, Kearns-Sayre syndrome, myoclonic **epilepsy**, encephalopathy, cardiomyopathy, and lactic acidosis.

DETD . . . subject to treat or prevent neurodegenerative diseases. Such diseases and disorders may include, but are not limited to, Alzheimer's disease, **Huntington**'s disease, Parkinson's disease, **epilepsy**, and Down's syndrome,

DETD . . . tissues of the sympathetic nervous system (paraganglion and smooth muscle tissues), NDS-4 is believed to play a role in cancer, **mitochondrial** myopathies, and disorders of the sympathetic nervous system.

DETD . . . in one embodiment, NDS-4 or a fragment or derivative thereof may be administered to a subject to treat or prevent **mitochondrial** myopathies. Such conditions and diseases may include, but are not limited to, progressive external ophthalmoplegia, Kearns-Sayre syndrome, myoclonic **epilepsy**, encephalopathy, cardiomyopathy, and lactic acidosis.

DETD . . . nontraditional bases such as inosine, queosine, and wybutosine, as well as acetyl-, methyl-, thio-, and similarly modified forms of adenine, **cytidine**, guanine, thymine, and uridine which are not as easily recognized by endogenous endonucleases.

DETD . . . of such conditions or diseases include cancers of the heart,

breast, colon, and prostate, neurodegenerative diseases such as Alzheimer's and **Huntington**'s disease, immunological disorders such as anemias, asthma, systemic lupus, myasthenia gravis, diabetes mellitus, autoimmune thyroiditis, pancreatitis, ulcerative colitis, osteoporosis, glomerulonephritis; rheumatoid and osteoarthritis; and scleroderma, myopathies such as progressive external ophthalmoplegia, Kearns-Sayre syndrome, myoclonic **epilepsy**, encephalopathy, cardiomyopathy, and lactic acidosis, and disorders of the sympathetic nervous system such as hypertension, cardiovascular shock, arrhythmias, asthma, migraine. . .

L14 ANSWER 81 OF 84 USPATFULL
AN 1998:104731 USPATFULL
TI Method of protecting brain tissue from cerebral infarction subsequent to ischemia
IN Sandage, Bobby Winston, Acton, MA, United States
Fisher, Marc, Shrewsbury, MA, United States
Locke, Kenneth Walter, Littleton, MA, United States
PA Interneuron Pharmaceuticals, Inc., Lexington, MA, United States (U.S. corporation)
PI US 5801160 19980901
AI US 1997-820244 19970318 (8)
RLI Continuation of Ser. No. US 1995-399262, filed on 6 Mar 1995, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Cintins, Marianne M.; Assistant Examiner: Moezie, M.
LREP Lowe, Price, LeBlanc & Becker
CLMN Number of Claims: 11
ECL Exemplary Claim: 1
DRWN 1 Drawing Figure(s); 1 Drawing Page(s)
LN.CNT 497
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Methods and pharmaceutical compositions for reducing the extent of infarction, particularly cerebral infarction subsequent to cerebral ischemia.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUMM . . . Such disorders include thromboembolic or hemorrhagic stroke, cerebral vasospasm, hypoglycemia, cardiac arrest, and status epilepticus, and also may include schizophrenia, **epilepsy**, neurodegenerative disorders, Alzheimer's disease, and **Huntington**'s disease.
SUMM . . . Although the relative contribution of each potential mechanism to the reduction of infarct size is unknown, citicoline and its hydrolysis products--**cytidine** and choline--are believed to play important roles in the generation of phospholipids involved in membrane formation and repair. These compounds. . .
DETD . . . brain edema during cerebral infarction. In addition, free fatty acids have been observed, in vitro, to inhibit oxidative phosphorylation in **mitochondria**. Previous investigators have reported that exogenous citicoline administration can stimulate phosphatidylcholine synthesis and prevent free fatty acid release. Others investigating. . .
CLM What is claimed is:
. . . protecting brain tissue from cerebral infarction subsequent to ischemia comprising administering an effective amount of citicoline, excluding effective amounts of **cytidine** diphosphoethanolamine, **cytidine** diphospho-N-methylethanolamine, **cytidine** diphospho-N,N-dimethylethanolamine, or mixtures thereof, to a subject in need thereof such that the extent of cerebral infarction subsequent to ischemia. . .

L14 ANSWER 82 OF 84 USPATFULL
AN 1998:88644 USPATFULL
TI F.sub.0 ATP synthase subunit
IN Hillman, Jennifer L., Mountain View, CA, United States

Goli, Surya K., Sunnyvale, CA, United States
PA Incyte Pharmaceuticals, Inc., Palo Alto, CA, United States (U.S. corporation)
PI US 5786150 19980728
AI US 1997-815177 19970311 (8)
DT Utility
FS Granted
EXNAM Primary Examiner: Patterson, Jr., Charles L.
LREP Billings, Lucy J., Mohan-Peterson, SheelaIncyte Pharmceuticals
CLMN Number of Claims: 10
ECL Exemplary Claim: 1
DRWN 4 Drawing Figure(s); 3 Drawing Page(s)
LN.CNT 1940
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides a human ATP synthase subunit (ASYS) and polynucleotides which encode ASYS. The invention also provides expression vectors, host cells, agonists, antisense molecules, antibodies, or antagonists. The invention also provides methods for producing ASYS and for treating disorders associated with expression of ASYS.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUMM The **mitochondrial** electron transport (or respiratory) chain is a series of enzyme complexes in the **mitochondrial** membrane that is responsible for the transport of electrons from NADH to oxygen and the coupling of this oxidation to. . .
SUMM . . . this chain and serves as a reversible coupling device that interconverts the energies of an electrochemical proton gradient across the **mitochondrial** membrane into either the synthesis or hydrolysis of ATP. This gradient is produced by other enzymes of the respiratory chain. . . oxygen. When the cell's energy demands are high, electron transport from NADH to oxygen generates an electrochemical gradient across the **mitochondrial** membrane. Proton translocation from the outer to the inner side of the membrane drives the synthesis of ATP. Under conditions. . . gradient is reversed and ATP synthase hydrolyzes ATP. The energy of hydrolysis is used to pump protons out of the **mitochondrial** matrix.
SUMM . . . an ATPase inhibitor protein, IF.sub.1) comprise the globular catalytic F.sub.1 ATPase portion of the complex, which lies outside of the **mitochondrial** membrane. The remaining ten polypeptides (subunits a, b, c, d, e, f, g, F6, OSCP, and A6L) comprise the proton-translocating,. . . chain, all but two of the polypeptide subunits of ATP synthase are nuclear gene products that are imported into the **mitochondria**; a and A6L are products of **mitochondrial** genes. Enzyme complexes similar to mammalian ATP synthase are found in all cell types and in chloroplast and bacterial membranes.. . .
DETD . . . to the initiator methionine that is acetylated in the bovine f subunit as a signal directing the protein to the **mitochondria**. As illustrated by FIGS. 3A and 3B, ASYS and bovine subunit f have rather similar hydrophobicity plots. In particular, a. . .
DETD . . . a subject to treat a myopathy. Myopathies may include, but are not limited to, progressive external ophthalmoplegia, Kearns-Sayre syndrome, myoclonic **epilepsy**, encephalopathy, cardiomyopathy, and lactic acidosis.
DETD . . . administered to a subject to treat a neurological disorder. Such disorders may include, but are not limited to, Alzheimer's disease, **Huntington**'s disease, Parkinson's disease, **epilepsy**, Down's syndrome, dementia, multiple sclerosis, and amyotrophic lateral sclerosis.
DETD . . . nontraditional bases such as inosine, queosine, and wybutosine, as well as acetyl-, methyl-, thio-, and similarly modified forms of adenine, **cytidine**, guanine, thymine, and uridine which are not as easily recognized by endogenous endonucleases.
DETD . . . with expression of ASYS. Examples of such conditions or diseases include myopathies such as progressive external ophthalmoplegia, Kearns-Sayre syndrome, myoclonic **epilepsy**,

encephalopathy, cardiomyopathy, and lactic acidosis; neurological disorders such as Alzheimer's disease, **Huntington**'s disease, Parkinson's disease, **epilepsy**, Down's syndrome, dementia, multiple sclerosis, and amyotrophic lateral sclerosis; cancers such as adenocarcinoma, sarcoma, melanoma, lymphoma, leukemia, and myeloma; and. . .

DETD . . . measured when F.sub.0 is reconstituted with the F.sub.1 ATPase and incubated together with a submitochondrial particle fraction prepared from bovine **mitochondria** which provides a source of electron transport from NADH to O.sub.2. ASYS is first incorporated into a reconstituted F.sub.0 molecule,. . . reconstituted with F.sub.1 ATPase to form a functional ATP synthase. Bovine submitochondrial particles are then prepared by sonication of intact **mitochondria** and isolated from the preparation by differential centrifugation. The assay is performed by incubating the reconstituted ATP synthase, submitochondrial particles,. . .

L14 ANSWER 83 OF 84 USPATFULL
AN 1998:65037 USPATFULL
TI CDNA encoding a human ATP synthase Fo subunit (ASYSD)
IN Hillman, Jennifer L., Mountain View, CA, United States
Goli, Surya K., Sunnyvale, CA, United States
PA Incyte Pharmaceuticals, Inc., Palo Alto, CA, United States (U.S. corporation)
PI US 5763248 19980609
AI US 1997-948195 19971009 (8)
RLI Continuation of Ser. No. US 1997-819395, filed on 17 Mar 1997, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: LeGuyader, John L.; Assistant Examiner: Wang, Andrew
LREP Billings, Lucy J.
CLMN Number of Claims: 6
ECL Exemplary Claim: 1
DRWN 5 Drawing Figure(s); 4 Drawing Page(s)
LN.CNT 1963
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides a human ATP synthase d subunit (ASYSD) and polynucleotides which encode ASYSD. The invention also provides expression vectors, host cells, agonists, antisense molecules, antibodies, or antagonists. The invention also provides methods for producing ASYSD and for treating disorders associated with expression of ASYSD.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUMM The **mitochondrial** electron transport (or respiratory) chain is a series of enzyme complexes in the **mitochondrial** membrane that is responsible for the transport of electrons from NADH to oxygen and the coupling of this oxidation to. . .

SUMM . . . this chain and serves as a reversible coupling device that interconverts the energies of an electrochemical proton gradient across the **mitochondrial** membrane into either the synthesis or hydrolysis of ATP. This gradient is produced by other enzymes of the respiratory chain. . . oxygen. When the cell's energy demands are high, electron transport from NADH to oxygen generates an electrochemical gradient across the **mitochondrial** membrane. Proton translocation from the outer to the inner side of the membrane drives the synthesis of ATP. Under conditions. . . gradient is reversed and ATP synthase hydrolyzes ATP. The energy of hydrolysis is used to pump protons out of the **mitochondrial** matrix.

SUMM . . . the F.sub.1 portion of which is catalytic and synthesizes or hydrolyzes ATP. The mammalian ATP synthase complex from bovine heart **mitochondria** consists of sixteen different polypeptides (Walker, J. E. and Collinson, T. R. (1994) FEBS Lett.346: 39-43). Six of these polypeptides. . . an ATPase inhibitor protein, IF.sub.1) comprise the globular catalytic F.sub.1 ATPase portion of the complex, which lies outside of the **mitochondrial** membrane. The remaining ten

polypeptides (subunits a, b, c, d, e, f, g, F6, OSCP, and A6L) comprise the proton-translocating,. . .

SUMM . . . chain, all but two of the polypeptide subunits of ATP synthase are nuclear gene products that are imported into the **mitochondria**; subunits a and A6L are products of **mitochondrial** genes. Enzyme complexes similar to mammalian ATP synthase are found in all cell types and in chloroplast and bacterial membranes.. . .

DETD . . . ASYSD extending from M1 to E18 is regarded as a noncleavable signal peptide directing the nuclear encoded protein to the **mitochondria** and is virtually identical to that in the bovine and rat d subunits. The 20 amino acid sequence extending between. . .

DETD Chemical and structural homology exists among ASYSD and ATP synthase d subunit from bovine and rat **mitochondria**. In addition, northern analysis shows the expression of ASYSD in cancerous tissues and immortalized cell lines, brain and neural tissue,. . .

DETD . . . administered to a subject to treat a neurodegenerative disease. Such diseases may include, but are not limited to, Alzheimer's disease, **Huntington**'s disease, Parkinson's disease, **epilepsy**, Down's syndrome, dementia, multiple sclerosis, and amyotrophic lateral sclerosis.

DETD . . . a subject to treat a myopathy. Myopathies may include, but are not limited to, progressive external ophthalmoplegia, Kearns-Sayre syndrome, myoclonic **epilepsy**, encephalopathy, cardiomyopathy, and lactic acidosis.

DETD . . . nontraditional bases such as inosine, queosine, and wybutosine, as well as acetyl-, methyl-, thio-, and similarly modified forms of adenine, **cytidine**, guanine, thymine, and uridine which are not as easily recognized by endogenous endonucleases.

DETD . . . which are associated with expression of ASYSD. Examples of such conditions or diseases include neurodegenerative diseases such as Alzheimer's disease, **Huntington**'s disease, Parkinson's disease, **epilepsy**, Down's syndrome, dementia, multiple sclerosis, and amyotrophic lateral sclerosis; myopathies such as progressive external ophthalmoplegia, Kearns-Sayre syndrome, myoclonic **epilepsy**, encephalopathy, cardiomyopathy, and lactic acidosis; cancer of the colon, pancreas, ovaries, brain, bladder, blood, intestine, uterus, stomach, breast, prostate, spleen,. . .

DETD . . . measured when F.sub.0 is reconstituted with the F.sub.1 ATPase and incubated together with a submitochondrial particle fraction prepared from bovine **mitochondria** which provides a source of electron transport from NADH to O.sub.2. ASYSD is first incorporated into a reconstituted F.sub.o molecule,. . . reconstituted with F.sub.1 ATPase to form a functional ATP synthase. Bovine submitochondrial particles are then prepared by sonication of intact **mitochondria** and isolated from the preparation by differential centrifugation. The assay is performed by incubating the reconstituted ATP synthase, submitochondrial particles,. . .

L14 ANSWER 84 OF 84 USPATFULL

AN 1998:57735 USPATFULL

TI CDNA encoding a human phospholemman-like protein (HPLP)

IN Bandman, Olga, 366 Anna Ave., Mountain View, CA, United States 94043
Goli, Surya K., 620 Iris Ave. #338, Sunnyvale, CA, United States 94086

PI US 5756310 19980526

AI US 1996-725531 19961003 (8)

DT Utility

FS Granted

EXNAM Primary Examiner: LeGuyader, John L.; Assistant Examiner: Wang, Andrew

LREP Billings, Lucy J.

CLMN Number of Claims: 6

ECL Exemplary Claim: 1

DRWN 4 Drawing Figure(s); 4 Drawing Page(s)

LN.CNT 1828

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention provides a novel human phospholemman-like protein (HPLP) and the polynucleotides which identify and encode HPLP. The

invention provides for genetically engineered expression vectors and host cells comprising the nucleic acid sequence encoding HPLP and for a method for producing the protein. The invention also provides pharmaceutical compositions containing HPLP and the use of such compositions for the prevention or treatment of diseases associated with the expression of HPLP. Additionally, the invention provides antisense molecules to HPLP and their use in the treatment of diseases associated with the expression of HPLP. The invention also provides diagnostic assays which utilize polynucleotides which hybridize with naturally occurring sequences encoding HPLP and antibodies which specifically bind to the protein.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

DETD . . . limited to, defects in nerve signal transmission, membrane potential generation, or fluid volume regulation, such as Alzheimer's disease, Parkinson's disease, **Huntington**'s disease, amyotrophic lateral sclerosis, and hydrocephalus.

DETD . . . nontraditional bases such as inosine, queosine and wybutosine as well as acetyl-, methyl-, thio- and similarly modified forms of adenine, **cytidine**, guanine, thymine, and uridine which are not as easily recognized by endogenous endonucleases.

DETD . . . by monitoring efflux of Cl.sup.- or K.sup.+ ions from vesicles containing HPLP subjected to a transmembrane ion potential. HPLP and **mitochondrial** cytochrome C oxidase, a proton pump, are reconstituted into lipid vesicles by sonication. .sup.36 Cl.sup.- or .sup.42 K.sup.+ is then. . .

=>

SWER 1 OF 3 CAPLUS COPYRIGHT 2002 ACS
AN 2000:608584 CAPLUS
DN 133:187987
TI Methods using pyrimidine-based nucleosides for treatment of mitochondrial disorders
IN Naviaux, Robert K.
PA The Regents of the University of California, USA
SO PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000050043	A1	20000831	WO 2000-US4663	20000223
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1171137	A1	20020116	EP 2000-910321	20000223
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRAI US 1999-121588P P 19990223
WO 2000-US4663 W 20000223
OS MARPAT 133:187987
AB Methods are provided for the treatment of mitochondrial disorders. The methods include the administration of a pyrimidine-based nucleoside, e.g. **triacetyluridine**. Also provided are methods of reducing or eliminating symptoms assocd. with mitochondrial disorders. Mitochondrial disorders particularly appropriate for treatment include those attributable to a deficiency of one or more pyrimidines.
RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
AB Methods are provided for the treatment of mitochondrial disorders. The methods include the administration of a pyrimidine-based nucleoside, e.g. **triacetyluridine**. Also provided are methods of reducing or eliminating symptoms assocd. with mitochondrial disorders. Mitochondrial disorders particularly appropriate for treatment include those attributable to a deficiency of one or more pyrimidines.
ST pyrimidine nucleoside deriv mitochondrial disorder treatment; **triacetyluridine** mitochondrial disorder treatment
IT Disease, animal
(**Asperger** syndrome with declines during infection; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
IT Mental disorder
(**autism**, **autism** with declines during infection; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
IT Infection
(refractory epilepsy or **Asperger** syndrome or **autism** with declines during infection; pyrimidine-based nucleoside for treatment of mitochondrial disorder)

L19 ANSWER 2 OF 3 USPATFULL
AN 2001:139534 USPATFULL
TI Compositions and methods for treatment of mitochondrial diseases
IN von Borstel, Reid W., Potomac, MD, United States
PA Pro-Neuron, Inc. (U.S. corporation)
PI US 2001016576 A1 20010823
AI US 2001-838136 A1 20010420 (9)
RLI Continuation of Ser. No. US 1998-144096, filed on 31 Aug 1998, PENDING
DT Utility
FS APPLICATION

LREP Nixon & Vanderhye P.C., 8th Floor, 1100 N. Glebe Rd., Arlington, VA, 22201
CLMN Number of Claims: 46
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1390
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Compounds, compositions, and methods are provided for treatment of disorders related to mitochondrial dysfunction. The methods comprise administering to a mammal a composition containing pyrimidine nucleotide precursors in amounts sufficient to treat symptoms resulting from mitochondrial respiratory chain deficiencies.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
DETD . . . the invention are short-chain (2 to 6 carbon atoms) fatty acid esters of uridine or cytidine. Particularly advantageous compounds are **triacetyluridine** or triacetylcytidine. Such compounds have better oral bioavailabilty than the parent nucleosides, and are rapidly deacetylated following absorption after oral. . .
DETD . . . circuits, resulting in delayed or arrested development of neuropsychological functions like language, motor, social, executive function, and cognitive skills. In **autism** for example, magnetic resonance spectroscopy measurements of cerebral phosphate compounds indicates that there is global undersynthesis of membranes and membrane. . .
DETD . . . Syndrome, pervasive developmental delay (or PDD-NOS: "pervasive developmental delay - not otherwise specified" to distinguish it from specific subcategories like **autism**), **autism**, **Asperger**'s Syndrome, and Attention Deficit/Hyperactivity Disorder (**ADHD**), which is becoming recognized as a delay or lag in development of neural circuitry underlying executive functions.
DETD . . . for treating patients with neurodevelopmental delays involving motor, language, executive function, and cognitive skills. Current treatments for such conditions, e.g. **ADHD**, involve amphetamine-like stimulants that enhance neurotransmission in some affected underdeveloped circuits, but such agents, which may improve control of disruptive. . .
DETD [0158] Example 5 illustrates the protective effect of oral **triacetyluridine** in protecting against taxol-induced neuropathy.
DETD [0183] Example 1: Treatment of a multisystem mitochondrial disorder with **triacetyluridine**
DETD [0185] After beginning treatment with 0.05 mg/kg/day of oral **triacetyluridine**, and for a duration of at least 6 months, this patient has not had seizures or migraines; her paresthesias related. . . to void spontaneously on most days, requiring catheterization only once or twice per week. After 6 weeks of treatment with **triacetyluridine**, this patient was able to walk a full mile, which she has been unable to do for the past two. . . tachycardia with a heart rate greater than 140 bpm occurred upon simple rise to stand, and after 6 weeks of **triacetyluridine**, tachycardia occurred only on hills and stairs. Her sensorium has cleared and memory deficits have improved markedly.
DETD [0188] The transient shortening of this patient's menstrual cycle is interpreted as an improvement of ovarian function caused by **triacetyluridine** in the face of excessive hormonal stimulation by which the neuroendocrine system was attempting to compensate for ovarian dysfunction. Feedback. . .
DETD [0191] In the first three days after beginning treatment with oral **triacetyluridine** (initially at a dose of 0.05 g/kg/day, and incrementally increased to 0.1 and then 0.24 glkg/day over the course of. . . some recurrence of seizures especially during episodes of infection, though at a much lower frequency than prior to treatment with **triacetyluridine**. This patient has been able to return to school and resume active participation in sports. His appetite, cognitive function, and. . .
DETD . . . acidosis requiring intravenous administration of 25 mEq per day of sodium bicarbonate. Within several hours after beginning intragastric

treatment with **triacetyluridine** at 0.1 g/mg/day, her renal tubular acidosis resolved and supplementary bicarbonate was no longer required to normalize blood pH. **Triacetyluridine** also resulted in rapid normalization of elevated circulating amino acid concentrations, and maintained lactic acid at low levels after withdrawal. . .

DETD [0195] A 4.5 year-old girl with epilepsy, ataxia, language delay, and fat intolerance, and dicarboxylic aciduria was treated with **triacetyluridine** at a daily dose of 0.1 to 0.3 g/kg/day. Such treatment resulted in a 50% decline in seizure frequency, improvement. . .

DETD . . . An additional group of 10 mice received injections of vehicle alone. One of the groups of taxol-treated mice received oral **triacetyluridine**, 4000 mg/kg b.i.d. Nine days after the initiation of taxol treatments, nociceptive sensory deficits were tested by determining tail-flick latency. . .

Group:	Tail flick latency
Control (no taxol)	10.8 .+-. 0.5 seconds
Taxol	16.0 .+-. 3.1 seconds
Taxol + **triacetyluridine**	11.9 .+-. 0.7 seconds

DETD [0199] Taxol treatment impaired responses to painful stimuli as an index of toxic sensory neuropathy. Oral **triacetyluridine** treatment significantly attenuated taxol-induced alterations in tail-flick latency.

CLM What is claimed is:
40. A method as in claim 36 wherein said developmental delay is **autism**.

L19 ANSWER 3 OF 3 USPATFULL
AN 2001:100342 USPATFULL
TI COMPOSITIONS AND METHODS FOR TREATMENT OF MITOCHONDRIAL DISEASES
IN VON BORSTEL, REID W., POTOMAC, MD, United States
PI US 2001005719 A1 20010628
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DT Utility
FS APPLICATION
LREP NIXON & VANDERHYE, 1100 N. GLEBE ROAD, 8TH FLOOR, ARLINGTON, VA, 22201
CLMN Number of Claims: 46
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1402
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Compounds, compositions, and methods are provided for treatment of disorders related to mitochondrial dysfunction. The methods comprise administering to a mammal a composition containing pyrimidine nucleotide precursors in amounts sufficient to treat symptoms resulting from mitochondrial respiratory chain deficiencies.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUMM . . . the invention are short-chain (2 to 6 carbon atoms) fatty acid esters of uridine or cytidine. Particularly advantageous compounds are **triacetyluridine** or triacetylcytidine. Such compounds have better oral bioavailability than the parent nucleosides, and are rapidly deacetylated following absorption after oral. . .

SUMM . . . circuits, resulting in delayed or arrested development of neuropsychological functions like language, motor, social, executive function, and cognitive skills. In **autism** for example, magnetic resonance spectroscopy measurements of cerebral phosphate compounds indicates that there is global undersynthesis of membranes and membrane. . .

SUMM . . . include Rett's Syndrome, pervasive developmental delay (or PDD-NOS: "pervasive developmental delay--not otherwise specified" to distinguish it from specific subcategories like **autism**),

autism, **Asperger**'s Syndrome, and Attention Deficit/Hyperactivity Disorder (**ADHD**), which is becoming recognized as a delay or lag in development of neural circuitry underlying executive functions.

SUMM . . . for treating patients with neurodevelopmental delays involving motor, language, executive function, and cognitive skills. Current treatments for such conditions, e.g. **ADHD**, involve amphetamine-like stimulants that enhance neurotransmission in some affected underdeveloped circuits, but such agents, which may improve control of disruptive. . .

SUMM [0151] Example 5 illustrates the protective effect of oral **triacetyluridine** in protecting against taxol-induced neuropathy.

DETD Treatment of a Multisystem Mitochondrial Disorder with **Triacetyluridine**

DETD [0173] After beginning treatment with 0.05 mg/kg/day of oral **triacetyluridine**, and for a duration of at least 6 months, this patient has not had seizures or migraines; her paresthesias related. . . to void spontaneously on most days, requiring catheterization only once or twice per week. After 6 weeks of treatment with **triacetyluridine**, this patient was able to walk a full mile, which she has been unable to do for the past two. . . tachycardia with a heart rate greater than 140 bpm occurred upon simple rise to stand, and after 6 weeks of **triacetyluridine**, tachycardia occurred only on hills and stairs. Her sensorium has cleared and memory deficits have improved markedly.

DETD [0176] The transient shortening of this patient's menstrual cycle is interpreted as an improvement of ovarian function caused by **triacetyluridine** in the face of excessive hormonal stimulation by which the neuroendocrine system was attempting to compensate for ovarian dysfunction. Feedback. . .

DETD [0178] In the first three days after beginning treatment with oral **triacetyluridine** (initially at a dose of 0.05 g/kg/day, and incrementally increased to 0.1 and then 0.24 g/kg/day over the course of. . . some recurrence of seizures especially during episodes of infection, though at a much lower frequency than prior to treatment with **triacetyluridine**. This patient has been able to return to school and resume active participation in sports. His appetite, cognitive function, and. . .

DETD . . . acidosis requiring intravenous administration of 25 mEq per day of sodium bicarbonate. Within several hours after beginning intragastric treatment with **triacetyluridine** at 0.1 g/mg/day, her renal tubular acidosis resolved and supplementary bicarbonate was no longer required to normalize blood pH. **Triacetyluridine** also resulted in rapid normalization of elevated circulating amino acid concentrations, and maintained lactic acid at low levels after withdrawal. . .

DETD [0180] A 4.5 year-old girl with epilepsy, ataxia, language delay, and fat intolerance, and dicarboxylic aciduria was treated with **triacetyluridine** at a daily dose of 0.1 to 0.3 g/kg/day. Such treatment resulted in a 50% decline in seizure frequency, improvement. . .

DETD . . . An additional group of 10 mice received injections of vehicle alone. One of the groups of taxol-treated mice received oral **triacetyluridine**, 4000 mg/kg b.i.d. Nine days after the initiation of taxol treatments, nociceptive sensory deficits were tested by determining tail-flick latency. . .

DETD [0186] Taxol+**triacetyluridine** 11.9.+-.0.7 seconds

DETD [0187] Taxol treatment impaired responses to painful stimuli as an index of toxic sensory neuropathy. Oral **triacetyluridine** treatment significantly attenuated taxol-induced alterations in tail-flick latency.

CLM What is claimed is:

40. A method as in claim 36 wherein said developmental delay is **autism**.